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DERMOID CYSTS AND TERATOMATA OF THE MEDIASTINUM*

With Report of A Case

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THE report of a case of dermoid cyst of the anterior mediastinum at the Boston City Hospital may be of interest because of the rarity of the disease, the large size of the tumor, the rôle played by infection, and the surgical cure affected by a two-stage operation, preceded by drainage.

The subject has been covered adequately by the reviews and reports of Aurousseau[1], Christian[2, 3], Hertzler[4], Harris[5], and Heuer[6]. Heuer's critical review of the entire series of cases up to January 1926 deletes the subject of doubtful cases and places the total number at 135. Since this review, the publication of a series of seventeen cases surgically treated intrathoracic tumors by Harrington[7] discloses three definitely proved cases of teratomata. Including our case the total number is 139 at the present writing.

A historical survey reveals several facts of interest. The first mediastinal dermoid to be reported was that of Gordon in 1825[8]. The patient was a young woman in whom the mediastinal tumor presented in both supraclavicular regions, going on to spontaneous rupture and death some time later. The lesion was discovered at autopsy witnessed by the father of the patient. The term "dermoid" was introduced by Leblanc[9]. The distinction between dermoid cysts and teratomata was emphasized by Lebert[10]. The first complete resection of a mediastinal dermoid cyst was accomplished by Bastianelli in 1893[11]. The advance in the surgical treatment of this and similar conditions is shown by Harrington's[7] series of intrathoracic tumors among which were three proved and successfully treated cases of teratomata.

The genesis of dermoid growths is by no means clear. The accepted fact of tumor development upon misplaced fetal tissues leaves the mechanism of the displacement unanswered. In most cases of mediastinal dermoid it would seem that Christian's[2] view of branchiogenic origin is plausible. He states that the great complexity of development that takes place in the neck favors misplacement of portions of the germinal layers. Such fetal inclusions are thought to descend into the thorax along with the heart and thymus. The presence of thyroid and thymus tissues in many of these growths is strong supportive evidence. Rare instances, however, of the presence of intestinal tissue in these growths (bearing strong resemblance to thyroid gland structure) cannot be explained.

Pathologically these tumors have been classified into three groups by Christian[2]. The first includes true dermoid cysts which are derived from ectodermal structures alone and are, therefore, of slight complexity. Such derivatives as epithelium, cartilage, bone in form of teeth, alveolar processes, etc., are to be found in this type of dermoid. The second group represents true teratomata derived from all three germinal layers, giving a more complex structure microscopically. The third group includes malignant degeneration, either cancerous or sarcomatous, of the simple dermoid cysts or teratomatous growths. Histologically the first group shows a cyst wall lined with epidermis, hair follicles, sebaceous glands and sometimes sweat glands. Polypoid excrescences of varying proportions may protrude into the cyst cavity and are found to be composed of fatty tissue covered with stratified epithelium. As stated above, bone, teeth, and cartilage are found commonly in this type of dermoid. The contents of the cyst may be sebaceous material with hairs, or, less characteristically, a cloudy brownish fluid containing cholesterin crystals. Pyogenic infection of the cyst contents is a frequent complication. The second group will show, as alluded to above, thyroid, thymus, intestinal and ganglionic tissues.

These tumors may attain surprisingly large proportions, that of Smith and Stone[12] with a measurement of 15 x 11 x 9 cm. being the largest on record. Our case, yielding a polypoid mass measuring 12 x 10 x 8 cm. forming only a part of the entire cyst structure, may be included with the largest. Harrington's[7] three cases showed equally large proportions, one of these measuring 15 x 10 cm.

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These growths have been classified on a regional basis by Duval[13] as follows: retrosternal, cervicosternal, mediastinothoracic and lateral thoracic. The cervicosternal type is of interest because of its presentation in the thyroid region as in the original case of Gordon[8]. Our case falls into the mediastinothoracic class.

The majority of these tumors occurs in early adult life, although cases have been reported in children. Smith and Stone[12] have reviewed eight cases occurring in children under 12 years of age. The relatively late manifestations of symptoms arising from a congenital lesion point to a slowness of growth further attested to by the large size of tumor often encountered. Most of these tumors are true dermoids which are slow growing and, therefore, the more amenable to surgical treatment.

There seems to be an even distribution of this tumor between the two sexes.

The symptoms may be classified as mechanical and infectious, either or both of which may appear in a given case. Mechanical or pressure symptoms occur in the form of cough, pain, dyspnea, dysphagia and sympathetic involvement; those due to infection by fever, chills, wasting, hemoptysis, and purulent sputum in event of rupture into a bronchus. Hemoptysis may be severe enough to be fatal. The importance of pain should be stressed. It may be localized over the growth or referred along the dorsal spinal nerves.

The findings in cases of mediastinal dermoids are in no way characteristic save for the rare presence of hair in the sputum, or, more commonly, in a chest tap. The clinical picture is mainly one of mediastinal tumor, the final differentiation of which is often solved only by operation. Tumor signs are manifested by a local swelling or bulge in the chest wall, Horner's syndrome, and clubbing of the fingers. The sputum in uncomplicated cases may be glassy mucoid or brownish mucoid. Frankly purulent sputum occurs with infection of the tumor and rupture into a bronchus. Other inflammatory signs may suggest lung abscess, pneumonia, with or without effusion or tuberculosis with or without cavitation.

Roentgenograms of the chest may be of positive value in some cases, while in others the reaction to inflammation in the lung parenchyma or in the pleura in the form of effusion obscures the underlying tumor. Lateral views and stereoscopic plates are, of course, helpful. Artificial pneumothorax is of definite value in locating and delineating some of these tumors. Where the inflammatory reaction is great, the x-ray evidence may suggest malignancy.

The diagnosis has been made preoperatively in a few cases, but as a rule the condition is suspected as one of localized empyema, lung abscess, bronchiectasis, pulmonary tuberculosis or malignancy. The coughing up of hair has served as a clue to preoperative diagnosis. In Hertzler's[4] case the resemblance of cervicosternal dermoid to an infected wen led to a correct preoperative diagnosis. It is conceivable that x-ray films may show well-formed teeth in some cases, thus giving a definite diagnostic lead. A chest tap, usually for suspected empyema, yielding a sebaceous or brownish fluid, ranks as the most common means of diagnosis. It is safe to say that a large number of these tumors are discovered accidentally either at operation or autopsy.

The treatment will depend upon the size and position of the tumor, the presence or absence of infection, and the condition of the patient. Heuer's[6] survey of the surgical results indicates the desirability of radical excision when conditions warrant. Sixty-nine of the one hundred and thirty-five cases reported were subjected to operative treatment while forty-six died untreated. The results of the sixty-nine surgically treated cases are tabulated in Table 1.

TABLE 1

RESULTS OF 69 SURGICALLY TREATED CASES OF DERMOIDS OF THE MEDIASTINUM — SUMMARIZED FROM HEUER

Procedure	No. Cases	Immediate Mortality		Subsequent Mortality		Unsatisfactory and Unknown Results		Cures	
		No.	%	No.	%	No.	%	No.	%
Pleurotomy	1	1	100	—	—	—	—	—	—
Incision and Drainage	34	9	26	4	12	16	48	5	14
Incomplete Resection*	12	2	17	—	—	5	41	5	41
Complete Resection	22	2	9	—	—	—	—	20	91
Totals	69	14	20	4	6	21	30	30	44

*Several cases previously drained.

Adding Harrington's three cases and our case to this list under the heading of complete resection and complete cure gives a total of 73 cases operated on, 26 with complete extirpation yielding cures in 24 or 92.3 per cent. The total number of cures from all procedures amounts to 34 or 46.5 per cent.

The operation of choice is transpleural thoracotomy with resection of one rib, section of the adjoining ribs, and complete extirpation of the tumor. The approach may be attempted through either anterior or posterior routes de-

pending upon the position of the tumor. Harrington's predilection for posterior approach in tumors of both the anterior and posterior mediastina is of interest. Infection will, of course, limit the procedure to drainage with or without marsupialization preliminary to subsequent removal. In rare cases a small dermoid, even though infected, may be extirpated completely.

CASE REPORT

M. H., a 22-year-old housemaid, was admitted to the Boston City Hospital on March 9, 1930 with the chief complaint of fever, malaise, and cough of two weeks' duration.

Five days before the onset of the present illness the patient had a tooth extracted under local anesthesia. Two weeks before admission she developed a sore throat which was associated with general malaise, fever, and cough. The cough was productive of moderate amounts of yellowish sputum. In addition she noticed that the left side of her neck was swollen. After the first day she tried to continue her work in spite of her malaise, loss of appetite, and occasional vomiting. The cough persisted with an increase of sputum up to four to six ounces a day. Three days before admission she became severely ill with an exacerbation of her cough, increase in amount of sputum, fever, and marked perspiration. In addition she developed a soreness in the anterior aspect of the right chest aggravated by coughing.

The family history disclosed no incidence of tuberculosis. The past history indicated that the patient was born in Ireland and came to this country 14 months ago. She was in the best of health up to the time of the present illness. She had had measles and mumps during childhood. Three years ago she had an attack of acute tonsillitis. Her teeth had always been poor. There were no cardiorespiratory symptoms in the past. The gastro-intestinal, genito-urinary, and neuromuscular systems caused no symptoms. Catamenia began at the age of 18, were regular, and normal in amount. Her best weight was 126 pounds one year ago. One month before admission she weighed 124 pounds.

On physical examination the patient showed a temperature of 101 degrees, pulse of 120, and respirations of 24. She was acutely ill, with flushed cheeks and slightly dilated alae nasi but no expiratory grunt. Cough was a prominent feature, yielding plentiful amounts of yellowish mucoid, lumpy, nonodorous sputum.

The head showed no positive findings. The pupils were equal, contracted, and did not react to light (codeine effect). There was no exophthalmos. The lips showed a herpetic lesion, and the tongue a marked gingivitis. The teeth were in very poor condition. Both tonsils were enlarged and acutely inflamed, discharging muco-purulent material. There was a marked pharyngitis. In the neck was felt a moderately enlarged anterior cervical gland on the left.

Examination of the chest disclosed a long type of thorax, symmetrical except for a slight prominence in the lower part of the right axilla. The expansion was equal in front while in the back the right side was found to lag slightly. Breathing was of the combined abdominothoracic type.

The heart showed a prominent apex impulse 2 cm. to the left of the nipple line. The rate was 125, the sounds were regular and no murmurs were heard. Percussion revealed no enlargement, the supracardiac dullness measuring 4 cm., the left border of dullness 10 cm. and the right border of dullness 1 cm. from the midsternal line. The pulses were equal and synchronous. The blood pressure was 130 mm. of mercury systolic and 68 mm. diastolic.

The left lung was normal to percussion and auscultation. The right lung posteriorly showed moist râles throughout with dullness, increased tactile fremitus and bronchial breathing in the middle third, and a pleural rub with distant bronchial breathing but normal tactile fremitus in the lower third. The axillary or lateral aspect of the right chest showed, from above downwards, increasing dullness to flatness with distant breath sounds, and decreased tactile fremitus. Anteriorly there was distinct flatness, absent tactile fremitus, absent breath sounds and coarse moist râles from the second rib downward.

The abdomen showed nothing abnormal. There was early clubbing of the fingers in both hands.

The laboratory revealed the following: On March 11 the red cell count was 5,240,000, hemoglobin 84% (Tallqvist), white cell count 16,800. The differential count with Wright's stain showed 66% polymorphonuclears, 22% lymphocytes, 12% monocytes. There

FIG. 1. Before thoracotomy.

was no anisocytosis, poikilocytosis, achromia, or immature cells. The platelets appeared to be definitely increased. The sputum showed no tubercle bacilli. The urine was acid, with a specific gravity of 1.020, and showed no albumin or sugar. The sediment showed a rare white blood cell. Both Kahn and Wassermann reactions were negative.

Roentgenograms on March 10 showed a density over the lower two-thirds of the right chest diagnosed as pneumonia by the x-ray service.

The clinical course for two weeks after admission was characterized by a septic temperature ranging from 101 to 104 degrees, a pulse rate of 120 and 140, and a respiratory rate of 30. The patient's cough persisted and yielded 4 to 6 ounces of the kind of sputum described above. Four additional sputum examinations showed no tubercle bacilli.

On March 24, 15 days after admission, a chest tap performed below the angle of the scapula on the right yielded a slightly cloudy, greenish yellow fluid with a cell count of 5,500 per cu. mm. and a differential count of 947 polymorphonuclears and 6% lymphocytes. Wright's stain showed many gram positive cocci in diplo and short chain arrangement.

On March 27, 18 days after admission, the opinion of both medical and surgical consultants was that the patient had an early empyema. A closed trocar thoracotomy was performed under novocaine anesthesia in the 8th interspace in the right posterior axillary line. The drainage from the thoracotomy was clear, straw-colored, and later proved to be sterile on culture. In view of the latter finding and the cessation of drainage the catheter was removed four days later. The patient's condition was improved, but she showed a slightly septic chart for three weeks after this drainage.

On April 18 an exploratory operation was decided upon after persistent findings of streptococci in the sputum and signs of fluid in the right mid-chest anteriorly which suggested an encapsulated empyema. Roentgenograms still showed pleural effusion and a possible cavity formation in the right mid-chest. At this operation, performed by Dr. E. D. Churchill, a portion of the third rib in the anterior axillary line

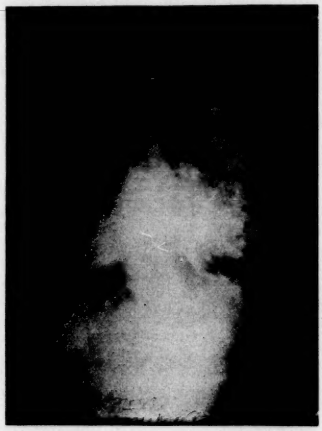

FIG. II. After thoracotomy.

was resected. Aspiration through apparently thickened pleura resulted in a small amount of creamy pus. Incision into this cavity revealed a large dermoid cyst containing sebaceous material and a large mass of hair. Because of the frank infection of the contents, the cavity was drained with rubber tubing.

There was considerable drainage following this procedure. Smear of the pus obtained at operation showed many polymorphonuclear leukocytes, a multitude of short chain streptococci and hemotoidin crystals. There was definite improvement of the patient's condition for the next two months.

On June 19, 1930, Dr. Churchill explored the cyst under gas-oxygen anesthesia. The fourth and fifth ribs were resected in addition to a further segment of the third rib. The cyst wall was cut through longitudinally, exposing a multiple pedunculated growth with hair and sebaceous material filling the interstices. The growth was apparently covered by cornified epithelium and was attached to the posterior aspect of the cyst wall. The cyst wall was marsupialized and the cavity filled with gauze, leaving the wound wide open.

The cyst, occupying an extrapleural situation from the mid-line to the anterior axillary line and from the second to the fifth ribs inclusive, was estimated as measuring six by eight inches.

The patient responded very well with a normal temperature chart for the first time during her illness.

On July 24, 1930, five weeks later, the final operative procedure of enucleation was performed by Dr. Robert C. Cochrane. Under gas-oxygen anesthesia a large segment of the second rib was removed from

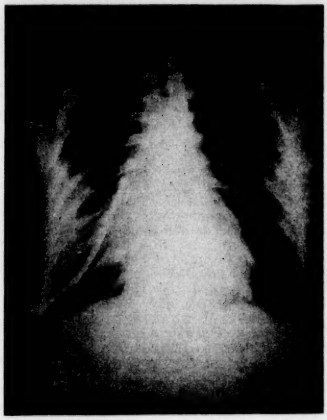

FIG. III. Tumor removed.

the right anterior chest giving access to the upper end of the growth where a line of cleavage was established. With both electrocautery and blunt dissection the cyst wall and the large attached lipomatous mass were dissected away from the pleura, pericardium, and anterior mediastinum. Small sections of the cyst wall were left behind in order to avoid opening into the pleural cavity. There was

FIG. IV. X-ray of tumor.

no evidence of bronchial communication. The vertical incision through the intercostal tissues was sutured except for its lower end, and the reflected breast was brought down to fill the cavity leaving only a small opening in the submammary crease for gauze drainage.

Pathologic examination revealed grossly a speci-

men consisting of a central mass of reddish gray tissue, approximately 8 x 12 x 10 cm. in size. The consistence was firm. From the central mass hung irregularly shaped oval appendages of soft consistence, apparently covered with epidermis. Portions of the main mass were cystic containing some yellowish sebaceous exudate. Small nodules of reddish tissue were found, from which were growing hairs. Three teeth could be distinguished growing from well-defined gum margins. The entire specimen was covered with a sebaceous material.

On microscopic examination, the wall of the cyst was found to be composed of fat and fibrous tissue, covered with a layer of stratified squamous epithelium. Numerous sebaceous glands and occasional hair follicles were connected with the epithelium, and a cluster of glands resembling coil glands was found. Embedded in the fat tissue was a piece of

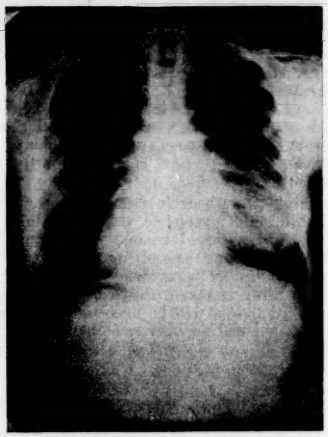

FIG. V. End result.

cartilage. Blood vessels in the fat tissue and connective tissue were fairly numerous. There was an infiltration throughout with lymphocytes, plasma cells and mast cells.

The patient stood this operation equally well and was out of bed in sixteen days. Her cough disappeared and the drainage was reduced rapidly in amount. In the remaining three months' stay her weight rose from 90 to 116 pounds. Chest plates showed clearing of the lower two-thirds of the right chest with no evidence of fluid. The patient was discharged October 23, 1930.

One year after her last operation the patient was in good health and actively employed in domestic work.

SUMMARY ON THE CASE HISTORY

A 22-year-old single housemaid without any previous respiratory trouble was admitted for cough and fever of two weeks' duration, commencing five days after a tooth extraction. She ran a septic course for two and one-half weeks with a productive cough. The signs were those of consolidation and fluid in the lower half of the right chest anteriorly. Three weeks after admission a chest tap in this region yielded frank pus, while rib resection opened into a cavity of sebaceous material and hair. Because of obvious infection rubber tube drainage was instituted. After eight weeks of drainage further exposure of the cyst was obtained by wide resection of two more ribs and marsupialization of the cyst wall. A pedunculated growth occupied most of the cyst cavity, with hair, sebaceous material and pus filling the crevices. Five weeks later enucleation of the growth and most of the cyst wall was performed. The patient made a completely satisfactory convalescence and was discharged 13 weeks after the last operation with a gain of 26 pounds in weight. One year later the patient was in good health and was back at domestic work, having gained 40 pounds.

COMMENT

From the point of view of symptomatology mediastinal dermoids fall roughly into two groups: one in which pain or pressure is a prominent feature, the other with infection predominating. This case falls clearly into the latter group. In fact, so marked were the acute infective features that the case was regarded as one of pneumonia or lung abscess, the latter particularly in view of the suggestive cavitation in the chest plate and history of tooth extraction, five days prior to the onset of symptoms.

Chronic infection, on the other hand, may lead to debility, loss of weight and infiltrative signs in the roentgenograms suggestive of malignancy. The tendency of intrathoracic tumor to cause irritative or infective reactions of this type may postpone surgery which would otherwise be curative. Exploratory surgery for undiagnosed or proved intrathoracic conditions, particularly tumors, will be more in evidence as thoracic surgery improves.

The ideal surgical treatment of mediastinal dermoids is complete resection in one stage. The established principle was modified in our case by the variant of infection. With a known streptococcus hemolyticus infection the dangers of empyema or pericarditis were too great to attempt resection in one stage. Simple tube drainage, although palliative, was not sufficient in this case. More extensive drainage was obtained by marsupialization of the cyst wall allowing adequate irrigation of the many-pocketed growth.

The resection of infected dermoids is notably difficult and requires painstaking dissection to accomplish complete removal without incident.

SUMMARY

A case of infected mediastino-thoracic dermoid cyst in a young woman of twenty-two is reported. The tumor was first drained and irrigated prior to a two-stage complete resection.

The growth was found to contain hair, sebaceous material, cartilage, alveolus formation and teeth. The patient has completely recovered except for an inconstant small sinus.

The presence of extensive infection determined the advisability of drainage preliminary to resection.

The literature up to date is reviewed.

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Discussion

Dr. Horace Binney, Boston, Mass.: I can discuss frankly this interesting communication on a very important subject only from a theoretical standpoint as I have never had a dermoid mediastinum and I think this is the only case I have ever seen.

I happened to go into the operating room at the City Hospital when Dr. Churchill was doing his second operation when the nature of the tumor was discovered, and it was certainly very interesting.

There are a few points that I should like to mention. Dr. Cochrane has spoken of the rarity of these conditions. The records of the City Hospital Pathological Department, which I hastily went through, show that since the present system of records has been carried on they have had only one dermoid cyst of the mediastinum in over thirty years.

The diagnosis, of course, is the difficult question and Dr. Cochrane has gone into that. For various reasons the early diagnosis, of course, is of very great importance and necessarily of considerable difficulty.

The points that I want to emphasize especially in regard to the early diagnosis are that, as Dr. Cochrane has said, some of these cases show referred pain. When the tumor is discovered, the history then has been gone over carefully and has shown that the patient has had some sort of referred pain for a considerable time.

I think that group of cases is not so common as those where the element of infection has entered and made symptoms perhaps much more clear. The example of referred pain I cannot quote in connection with dermoids, but Heuer mentions a very interesting case of mediastinal tumor which caused referred pain for twelve years before the nature of the condition was discovered.

That case I think is worth mentioning in this connection. The patient was a physician who had had right-sided abdominal pain of a fluctuating type for years, and who, fairly early in the course of his troubles, had had the appendix removed, which naturally gave no relief. It was not until he had an attack of influenza and an x-ray was taken some twelve years after the origin of his pain, that the tumor was discovered which occupied, in this case, the posterior mediastinum and which proved to be xanthoma upon removal. After removal of the tumor the man was entirely cured.

I think if we bear in mind these conditions of baffling and mysterious referred pain which affect perhaps the abdominal regions and also the arm, as being possibly of reflex origin or from pressure of a growth in the chest, so that an x-ray is taken, then early diagnosis in some of the cases will be made and the results of treatment will necessarily be better.

Dr. Cochrane mentioned Heuer's statistics which he had in his table. I have a few of them here and, with your permission, I will quote briefly the following ones which bring out the great advantage of early diagnosis.

If the diagnosis is made early, a complete removal can be done, whereas if the condition has gone on to infection, in most cases the complete removal in one stage is impossible and complications oftentimes make proper treatment very difficult.

Heuer found in the literature that in 22 cases complete removal had been carried out, with only two deaths; that is, in that group he had a mortality of only 9 per cent. and a complete cure in 91 per cent. Partial resection, which may have to be done in cases where the tumor is much larger and adherent, gave a mortality of 16 per cent. at operation, and 41 per cent. were cured. The less desirable operation is that of incision and drainage which had a mortality of 26 per cent. with only 14 per cent. cured. Dr. Cochrane is to be congratulated on his successful handling of this very difficult case.

CLINICAL ASPECTS OF THYROID MALIGNANCY*

BY HOWARD M. CLUTE, M.D.†

ALTHOUGH cancer of the thyroid gland is seen with relative frequency in a clinic in which numerous patients with thyroid disease are treated, it is, nevertheless, of such relatively rare occurrence in the practice of physicians not devoting a considerable portion of their time to the study of affections of this gland, that by them the significance of the precancerous lesions and of the early malignant tumors in the thyroid gland is, perhaps, not so fully appreciated as is desirable. Actual figures as to the frequency of malignancy in the thyroid gland are difficult to state. In the years 1916 to 1930, in the Lahey Clinic there have been 187 proven cases of thyroid cancer in 6,535 patients operated upon for thyroid gland disease. In addition to these 187 proven cases there have been many other patients who had thyroid malignancy which had advanced to such a stage that no operation was possible and hence no histologic proof of thyroid cancer was obtained. The known incidence of malignancy in this group of 6,535 patients, then, is 2.86% and the actual incidence of thyroid cancer, in our experience with thyroid disease, is, doubtless, definitely greater than this. While we appreciate the fact that a cross section of any community will show no such incidence of cancer of the thyroid gland as three per cent., nevertheless we must assume that there is a very definite danger of malignant degeneration in thyroid tumors as they exist throughout the country.

In a recent study of the thyroid malignancy in patients seen in the Lahey Clinic an attempt was made by Clute and Warren[1] to group these patients for the purpose of better prognosis and treatment under three headings. In Group I were placed the patients who had only low or potential malignancy, and in whom the chance of recurrence was relatively slight and the hope of cure was very great. In this group belonged the tumors arising primarily in fetal adenoma. Histologically these are adenomata with simple blood vessel invasion, or papillary cyst adenomata. Of these two types we have had 133 cases; all of these patients save six were followed for more than a year after operation, and the mortality rate from this disease was only 4½%. This is the group of patients in whom the diagnosis of malignancy frequently can only be made histologically and in whom the removal of the fetal adenoma followed by x-ray radiation gives an excellent prognosis.

In Group II we placed the patients who histologically showed an adenocarcinoma of either the papillary or the alveolar type. This group we consider of more serious malignancy than Group I and yet of a malignancy which allows a hope of cure. Clinically these patients may have an adenoma of the thyroid which has been present for some time but has recently undergone some increase in size and has, perhaps, become slightly adherent to the surrounding structures. In this group of cases the adenoma, on clinical examination, not infrequently feels hard and firm and suggests the possibility of malignancy. There were 21 patients in the group, with a mortality rate of 23.9%. These tumors are somewhat susceptible to x-ray treatment and this measure, combined with radical removal of the tumor, has in some cases resulted in freedom from recurrence of the trouble for as long as three years after the operation.

In Group III we have placed the patients whose tumors histologically were either small cell carcinoma, squamous cell carcinoma, giant cell carcinoma or fibrosarcoma. These patients, in our series, number thirty-three, of whom 82% have died. This is the group of most serious thyroid malignancy. Usually no adenoma is present before the tumor is noted, the onset and course of the disease are extremely rapid, metastases to the neck and lungs are early, radical operation is either impossible or of no avail, and x-ray treatment, as a general rule, does no particular good. Only four patients in this entire group are alive from one to three years after operation and in the majority of cases with a fatal termination death occurred within a few months of the origin of the tumor.

In certain textbooks dealing with diseases of the thyroid gland the symptoms and signs of thyroid malignancy are stated as follows: "In the patient's neck appears a rapidly growing tumor, which is hard, firm and deeply attached to the overlying and surrounding structures. Difficulty in breathing and swallowing are present; hoarseness occurs; metastases to the lungs and adjacent lymph nodes are frequent. The course is rapidly more and more unfavorable and death ensues usually from respiratory obstruction." Such a description of thyroid cancer is the picture of the last stages of malignancy arising in the thyroid gland. A patient presenting such a clinical picture can be readily diagnosed as having hopeless cancer of the thyroid beyond any present measures of treatment. Since there is so little that we can do for patients in this condition, either in the way of palliative or curative measures, it is but natural that for many years the general feeling amongst medical men has been that malignancy arising in the thyroid was an utterly hopeless condition which, fortunately, was usually of but short duration.

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As our information about malignancy in the thyroid gland increases, however, there are certain factors which make us much more hopeful in our dealings with this condition. Probably the most important of these facts is our knowledge that certainly 90% of all malignancy in the thyroid gland arises on the basis of a preëxisting adenoma of the thyroid. This knowledge, alone, should make the occurrence of fatal malignancy in the thyroid gland very definitely less frequent since it permits the early removal in many patients of the premalignant lesion.

Clinically we find two types of adenoma occurring in the thyroid gland. The first type—the so-called "colloid adenoma"—is really the result of a degenerative process occurring in an endemic or colloid goitre. Endemic goitre is distinctly a deficiency disease of the thyroid gland and is marked by a diffuse hypertrophy of the gland with colloid distention of the gland follicles. As these colloid glands go through the cycle of hyperplasia, involution and rest, degenerative changes in various follicles occur, and areas of thyroid tissue become separated by fibrous tissue. These areas, in time, develop into adenoma-like bodies containing varying degrees of colloid and thyroid tissue and surrounded by a fibrous tissue capsule and thus give rise to the nodular or multiple adenomatous type of endemic goitre. The second type of adenoma which is found in the thyroid gland is the so-called "fetal adenoma". These tumors should be considered as of a different nature than the degenerative colloid adenomata. They are made up of thyroid tissue cells in varying stages of development and are surrounded by a definite capsule. Their cells show hyperplasia, anaplasia, hypertrophy and frequently mitotic figures. Fetal adenomata must be looked upon as tumors of the thyroid gland and, therefore, as premalignant lesions of the thyroid gland.

Fetal adenomata are frequently found in a thyroid gland which is otherwise normal. They are, therefore, very commonly asymmetrically placed and involve but one small portion of a lobe or the isthmus. Colloid or degenerative adenomatous areas, so commonly found in endemic goitres, however, are scattered through the gland in a most irregular fashion. Usually they are innumerable. Unfortunately, in glands filled with numerous colloid adenomata commonly there are, in addition, one or more fetal adenomata. We must assume, therefore, when we examine a goitre in which there are either single or multiple adenomata that, in all probability, one or more of the tumors are fetal adenomata and of a precancerous nature. The significance of this fact is shown by a recent study of all single adenomata operated upon in recent years in the Clinic. Six per cent. of these patients showed the presence of malignant degeneration in an adenoma.

An immediate question which arises when we discover either a single adenoma or multiple adenomata in the thyroid gland is whether malignancy is already present. We have been repeatedly impressed with the fact that the pathologist will report malignancy in certain thyroid tumors which, to all the clinical methods of examination at our command, appear to be benign. On the other hand, in certain tumors of the thyroid gland the presence of malignancy is suspected on clinical examination by the definite firmness and fixation of the tumor and by a recent increase in its size. These are the only early signs of possible clinical malignant degeneration in a thyroid adenoma with which we are familiar and we must emphasize again that we very frequently are surprised to find malignancy reported by the pathologist in other adenomata of the thyroid that have been removed, which, on clinical examination, were soft, freely movable and had had no recent change in their size.

Pathologists, for some years, have been perplexed as to the correct diagnosis of malignancy when it is present in a fetal adenoma of the thyroid gland. These adenomata typically show many rapidly growing young thyroid cells with anaplasia, hyperplasia and mitotic figures. Such findings in any other tissue in the body are considered evidence of the rapid growth of cancer tissue. Yet experience has shown that many patients presenting such a histologic picture fail to show any clinical evidence of cancer. The problem was considerably simplified in 1924 by Allen Graham[2] of Cleveland, who stated that a finding which was significant of malignancy in fetal adenomata of the thyroid was the actual invasion of the lumen of blood vessels by strands of the tumor tissue. Blood vessel invasion has, therefore, been quite generally adopted by pathologists as definite evidence of malignancy in thyroid tumors and we have used this criterion in our diagnoses since 1927. In order to determine how frequently this finding of blood vessel invasion was accompanied by later evidence of thyroid cancer, Dr. Shields Warren investigated eleven hundred and fourteen specimens removed in this Clinic from thyroid adenomata during the years 1923-1928 before blood vessel invasion had been particularly searched for by the pathologists. In this group there were thirty-four tumors which were found to have definite blood vessel invasion and which would now be classed as malignant. All these thirty-four patients were followed and it was found that of the 34, two patients died later of undoubted metastases from thyroid cancer. In neither case was thyroid malignancy suspected at the original operation.

In our experience in all the patients who have had adenomata with blood vessel invasion and have later had a return of the malignant process, recurrence has occurred within a year of the time of the original operation. We have felt, in

view of this, that if such patients go a year after their operation without evidence of recurrence of the tumor, we may assume it is probable they will have no further trouble.

There is a second type of thyroid malignancy which may, or may not, arise on the basis of a preëxisting thyroid adenoma but which, nevertheless, differs very decidedly from the clinical picture of the malignant adenoma which we have just discussed. This type of malignancy differs in its mode of onset, in the rapidity of its course and termination, and in the clinical and histologic findings which are present.

The usual history in patients belonging to this second group is that they noted a swelling in the neck a relatively short time before coming for examination. Very commonly the swelling was first noted within a month or two months before admission and had rapidly increased in size. Difficulty in breathing occurs early in these patients, swallowing becomes difficult a little later, and hoarseness is frequent in the early course of the disease.

On examination the patient is found to have a hard, brawny, indurated, absolutely fixed tumor, arising in the thyroid gland and generally spreading downward toward the mediastinum. X-ray pictures may show metastases in the lungs or the hilum of the lung very early in the course of the disease and the regional lymph nodes are involved relatively soon after the tumor has been noted. Occasionally these tumors seem to be limited to an adenoma-like formation in part of one lobe, for a time, and this can be palpated as a definite localized swelling of the gland, which is very hard and firm and considerably fixed. Histologically these tumors are adenocarcinoma, small-cell or giant-cell carcinoma, or sarcocarcinoma in the great majority of cases.

In our experience with 187 cases of thyroid malignancy, 133 were primarily malignant adenomata of the thyroid gland and 54 were of this second type, including the various forms of carcinoma and carcinosarcoma of the thyroid gland. This latter group forms roughly one-third of the cases of thyroid malignancy that we have observed and they are a most serious group of cancer cases, since they advance to a fatal termination so rapidly, are frequently inoperable and respond so little to radiation therapy.

In our experience with this group of rapidly growing tumors of the thyroid gland, surgical excision, radical though it may be, is usually followed by a rapid recurrence of the disease. X-ray therapy has been of some value in holding certain cases in check, but the majority of the patients have been dead within six months of the time of the operation in spite of x-ray or surgery. Only a few have lived for as long as two years after the operation.

Clinically these two great groups of thyroid malignancy can usually be readily diagnosed. In the first group we have the history of an adenoma present for years with but slow increase in size; the absence of many pressure symptoms; the freedom from metastases; and the finding of either an apparently benign thyroid tumor or one with beginning firmness and fixation. In the second group we have a history of sudden appearance of a growth in the neck, or of the rapid enlargement of a tumor long present; the rapid development of serious symptoms such as choking, hoarseness, dysphagia and cough; the early appearance of metastases; and the finding on examination of a stony, hard, fixed, obviously malignant tumor in the thyroid area.

It is especially in the first group that our present knowledge permits us to reduce the incidence and mortality of thyroid cancer by the early removal of thyroid adenomata. It is in the second group of cases that the black picture of thyroid cancer so often painted arises.

SUMMARY

We may summarize, then, our clinical views upon malignancy of the thyroid gland as follows: Since 90% of thyroid malignancy arises on the basis of a preëxisting adenoma, this must be considered as the outstanding premalignant lesion in the thyroid. There are relatively few clinical findings by which an early malignant degeneration in a thyroid adenoma can be distinguished. Marked firmness and fixation of the adenoma are very suggestive of malignant changes. When a thyroid adenoma is removed and is found to show malignancy on histologic examination, postoperative x-ray therapy is desirable and, we believe, has a distinct value. If no recurrence of the malignancy occurs within a year of the time of the removal of the tumor, our experience goes to show that recurrence need not be expected at a later date.

The most serious types of thyroid malignancy are those which arise as a diffuse, rapidly spreading process in the thyroid gland and which are in many instances unrelated to the presence of any adenoma in the gland. In such cases there is a rapidly growing tumor, which early metastasizes to the adjacent lymph glands and to the lungs, and which is readily diagnosed on clinical examination as malignant because of its stony hardness, its fixation and its interference with breathing and swallowing. Surgery and x-ray treatment are of relatively slight avail under these conditions and the disease is rapidly progressive to a fatal termination.

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SOME CLINICAL ASPECTS OF DEFICIENCY DISEASES*

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INTRODUCTION

In recent years a number of advances have been made in understanding the various food deficiency disorders in man. The results of many investigations have shown that they occur not only following a restricted diet, but also during the course of conditions interfering with normal nutrition, such as chronic diarrhea, and when increased demands are made in the organism, as by pregnancy. It also has become evident that the composite clinical picture, which is frequently presented, is not the result of the lack of a single factor in the diet such as a vitamin, but rather the result of insufficient amounts of other essential food substances such as protein, iron, calcium, phosphorus and iodine.

An appreciation of this concept of multiple deficiency disorders in man is of importance to the clinician in the interpretation of the various disturbances encountered in patients and, when analyzed, such a syndrome is not surprising. Single deficiencies may be studied in animals only after the diet has been planned with meticulous care, but since the diet of man is never so arranged and is dictated largely by such factors as geographic location, class custom, habits, and the general economic status, it is only natural that diets which are deficient in one way may be deficient in others. That this is true is supported by numerous clinical observations. The object of this communication is to summarize from personal observations some of the clinical aspects of certain food deficiency disorders as they are encountered in man. For those interested in the general subject of food deficiencies, the recent papers of Minot[1] and Frank[2] should be consulted.

Before discussing the clinical features of deficiency diseases in detail, the conditions in which they occur are summarized in Table I. It is manifest from this table that the various deficiency disorders are brought about not only as a result of a restricted diet, but they also arise as a complication of many diseases.

TABLE I

CONDITIONS IN WHICH DEFICIENCY DISEASES DEVELOP

I *Keratomalacia*
- (1) Restricted diets
- (2) Chronic dysentery
- (3) Diabetes
- (4) Celiac disease
- (5) Tuberculosis of intestines
- (6) Ulcerative colitis

II. *Beriberi*
- (1) Restricted diets
- (2) Chronic dysentery
- (3) Diabetes
- (4) Pregnancy
- (5) Hyperthyroidism
- (6) Celiac disease

III. *Scurvy*
- (1) Restricted diets
- (2) Pernicious anemia
- (3) Chronic dysentery

IV. *Pellagra*
- (1) Inadequate diet
- (2) Carcinoma of stomach
- (3) Carcinoma of ileum
- (4) Tuberculosis of intestines
- (5) Chronic dysentery
- (6) Stricture of rectum
- (7) Carcinoma of colon
- (8) Ulcerative colitis
- (9) Pernicious anemia
- (10) Chronic alcoholism
- (11) Stricture esophagus
- (12) Pyloric obstruction
- (13) Gastro-enterostomy

V. *Rickets*
- (1) Inadequate diet
- (2) Celiac disease

VI. *Tetany*
- (1) Inadequate diet
- (2) Osteomalacia
- (3) Rickets
- (4) Sprue
- (5) Malabsorption of fat
- (6) Pregnancy
- (7) Lactation
- (8) Celiac disease

VII. *Osteoporosis*
- (1) Celiac disease of adults
- (2) Sprue
- (3) Pernicious anemia

VIII. *Osteomalacia*
- (1) Pregnancy
- (2) Inadequate diets
- (3) Hyperthyroidism

IX. *Edema Disease*
- (1) Inadequate diet
- (2) Chronic dysentery
- (3) Tuberculosis of intestines
- (4) Pernicious anemia
- (5) Diabetes mellitus
- (6) Pregnancy
- (7) Lactation
- (8) Pellagra

In Table II, I have summarized the personally observed cases, together with the conditions in which they appeared.

TABLE II

AUTHOR'S CASES OF DEFICIENCY DISEASES AND CONDITIONS IN WHICH THEY WERE OBSERVED

(1) *Keratomalacia*	6
(a) Chronic dysentery	3
(b) Tuberculosis of the intestines	2
(c) Inadequate diet	1

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(2) *Beriberi*		10
(a) Inadequate diets	8	
(b) Chronic dysentery	2	
(3) *Scurvy*		3
(4) *Hyperkeratosis Follicularis*		6
(a) Inadequate diets	4	
(b) Chronic dysentery	2	
(5) *Edema Disease*		17
(a) Inadequate diet	9	
(b) Chronic dysentery	6	
(c) Tuberculosis of the intestines	2	
(6) *Osteomalacia*		2
(7) *Pellagra*		15
(a) Pernicious anemia	2	
(b) Ulcerative colitis	3	
(c) Tuberculosis of the intestines	2	
(d) Chronic dysentery	2	
(e) Chronic alcoholism	1	
(f) Carcinoma of stomach	1	
(g) Restricted diets	4	

CLINICAL FEATURES OF DEFICIENCY DISORDERS

In diagram I the various clinical features of the deficiency disorders are shown, and they may be discussed briefly.

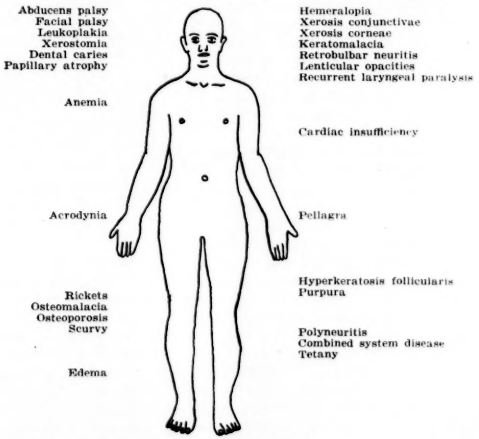

FIG. I. Diagram illustrating the various clinical features of Deficiency Disorders.

Hemeralopia, or night-blindness, is due to vitamin A deficiency. It is characterized by an inability of the patient to see in the evening, especially after sunset. It may occur alone or be associated with other lesions due to vitamin A insufficiency, such as xerosis conjunctivae, cornea, or keratomalacia. The diagnosis is made from the history because examination of the ocular fundi reveals nothing abnormal. Besides occurring with keratomalacia, it has been described in patients with beriberi[3] and edema disease[4], and in all of the older clinical descriptions of scurvy, night-blindness is usually included as one of the characteristic features of the disease. At present, it is known that this symptom does not necessarily occur in patients with scurvy unless the diet is deficient in vitamin A as well as vitamin C. For example, Salle and Rosenberg[5] observed hemeralopia very infrequently in the cases of scurvy they studied.

Retrobulbar neuritis with central scotoma has been described by Fernando[6] in patients from the Philippines with vitamin B deficiency, and recently Shimazono[7] has reported a number of cases from Japan. He points out that it is an extremely common condition in vitamin B deficiency and appears quite frequently during lactation in women. The cases of retrobulbar neuritis that are observed in chronic alcoholism and paranasal sinus infection should be investigated from this standpoint.

Paralysis of the recurrent laryngeal nerves in beriberi, either unilateral or bilateral, has been described by Fernando[8] and Miura[9]. The latter author has also described bilateral facial paralysis in similar cases. Abducens palsy and optic neuritis have been observed in the cases of beriberi reported by Little in Newfoundland[10].

Peripheral neuritis is the lesion usually attributed to a lack of vitamin B or F. There is nothing characteristic of this form of polyneuritis except that it disappears following an adequate diet. It is of importance to appreciate, however, that under the best of circumstances the recovery period may be slow. That

is to say, complete recovery from the neuritis may not be observed for 6 to 8 weeks, or even longer.

In recent years, combined systemic disease has been considered a deficiency disorder. This view gains support from the clinical observation of its occurrence in pellagra, pernicious anemia, also beriberi, lathyrism, ergotism, chronic dysentery, and carcinoma of the stomach. Animal experiments by Gildea, Kattwinkel, and Castle[11], and by Mellanby[12] have shown that lesions not unlike those in human cases of combined system disease can be produced by deficient diets. The precise nature of the deficiency is not definitely settled since Castle's results were obtained following a diet deficient especially in vitamin B, whereas Mellanby's results were observed on vitamin A deficient diets. At the present time, the fact of importance is that the lesions of subacute combined sclerosis have been produced in animals on deficient diets, and this disorder should, therefore, be considered a deficiency disease and should be studied from this viewpoint.

Apart from the conditions mentioned as signs of beriberi, Hoobler[13] has called attention to disturbances in infants which he feels are the result of a partial lack of vitamin B in the diet. These symptoms include irritability, anorexia, loss of weight, retardation of growth, and rigidity. All of these conditions have been observed to disappear following the addition of adequate amounts of vitamin B to the diet in the form of wheat germ and yeast. These observations emphasize the importance of giving optimum amounts of essential food substances to all patients.

Irritability of the central nervous system due to a low vitamin D intake and a resulting decrease in the blood calcium are commonly manifested by tetany. It is most often seen associated with rickets but is also observed in osteomalacia, celiac disease, sprue, fatty diarrhea, and during lactation. Liu[14] has reported a number of children in whom tetany without demonstrable bone changes was observed during the winter months. This was due to a lack of vitamin D and calcium in the diet. The cases of tetany resulting from vitamin D deficiency must be differentiated from those resulting from hypoparathyroidism, as described by Albright and Ellsworth[15] and Liu[16]. Relief of the tetany in vitamin D deficiency is obtained by supplying vitamin D and calcium, and, in the form due to hypoparathyroidism, by injecting parathyroid extract.

The changes in the skin resulting from deficiency diseases which merit attention are hyperkeratosis follicularis, the skin lesions of pellagra, and purpura.

Hyperkeratosis follicularis has been described alone[17] or associated with keratomalacia[17], scurvy, or edema disease. Frazier and Hu[17] have studied this lesion in detail and attribute the changes in the skin to a lack of vitamin A in the diet. The lesions are characterized by a hyperkeratosis about the hair follicles and are most commonly seen on the extensor surfaces of the arms and legs and over the abdomen. On histologic section there is evidence of atrophy of the sweat and sebaceous glands and a keratinization of the epithelium of the hair follicles, so that each follicle may project from the surface as a small spine. Many of these follicles show evidence of infection with suppuration and the formation of small ulcers. The infections disappear and the skin assumes a normal appearance after the patient takes cod liver oil for a number of weeks. These skin lesions have been considered characteristic of scurvy inasmuch as they are commonly observed in that disease and the petechial hemorrhages in the skin in scurvy are usually about the hair follicles. When, however, the skin of some patients with scurvy is examined, it is noted that the hemorrhages are very frequently present about the hair follicles without any evidence of hyperkeratosis and when the latter condition is present, it probably means a deficiency of vitamin A as well as vitamin C.

The skin lesions of pellagra are well defined and easily recognized. Of all the cases of deficiency diseases that occur sporadically, pellagra is probably one of the commonest. It may be seen in Table I that this disease has been observed under a great variety of circumstances. Recently Eusterman and O'Leary[57] have described its occurrence secondary to a variety of gastro-intestinal disorders and they emphasize the importance of disturbed function of the gastro-intestinal tract in predisposing patients to the development of this disease.

Purpuric lesions, aside from those observed in scurvy, are occasionally observed, such as the hemorrhages into the sclerae as recorded by Bürger[8] in edema disease, and I have seen a petechial eruption in the skin in similar patients.

The changes in eyes, such as pre-xerosis, xerosis conjunctivae and corneae, keratomalacia and lenticular opacities have been discussed in detail recently by Pillat[19], and those interested in a thorough and detailed study of this particular subject should consult his papers.

Some patients with vitamin B deficiency develop cardiac insufficiency. In a previous paper, I described the clinical course of a number of such patients[20]. Briefly, the patients who develop cardiac insufficiency with vitamin B deficiency are those who have slight involvement of the central nervous system and a preservation of muscular power. If they are able to carry on normal activities, a burden is placed on the heart which is already embarrassed by the deficiency of vitamin. This causes a failure of the myocardium. If the nervous system is extensively involved, so that a polyneuritis develops, the patient is unable to carry on normal activities. As a result, the burden of exercise is not placed on the heart and failure does not occur.

Exceptions to these observations are seen in infantile beriberi, in which cardiac insufficiency occurs without exercise. It is of importance, however, to appreciate the fact that a variety of inadequate diets are capable of producing such profound disturbances in the cardiovascular system that severe circulatory failure may appear.

Generalized edema with or without effusions into the serous cavities also results from inadequate diets and, as a rule, it follows a diet that is both quantitatively and qualitatively low in protein. This disorder has been commonly called edema disease, malnutrition edema, hunger edema, war or prison edema. The diagnosis is made from the presence of a generalized edema without other signs of cardiac or renal disease. In my experience it has always been associated with a decreased amount of total protein in the blood serum and recovery follows the ingestion of large amounts of protein in the diet.

Various alterations in the structure and growth of bone are observed commonly in rickets, osteomalacia and scurvy. The first two conditions result from vitamin D deficiency and the former is more common. Osteomalacia is less common but sporadic cases are observed such as the one reported recently by Gargill, Gilligan and Blumgart[21]. Rapid healing is usually observed in all of these patients following treatment with adequate diets. In some cases, however, it is necessary to give large amounts of vitamins in order to bring about healing. In the patient studied by Gargill, Gilligan and Blumgart, large doses of vitamins in the form of cod liver oil and oscodal had to be given before improvement occurred.

Of considerable importance to the clinician are the changes in the bones, known as osteoporosis, which occur as a result of the inadequate absorption of calcium salts. They have been observed in pernicious anemia, sprue, and celiac disease of adults, or fatty diarrhea. In these cases, the bones may become so brittle that spontaneous fractures take place. It is necessary in all such cases to examine the bones carefully with x-rays in order to determine the extent of the osteoporosis and the effects of treatment. The various conditions in which it has been observed are listed in Table I.

There are other conditions in man requiring further investigation from the point of view of dietary deficiency; for example, leukoplakia of the genito-urinary tract, and renal and bladder calculi. A few years ago, Osborne and Mendel[23] called attention to the fact that rats fed on diets deficient in vitamin A frequently developed urinary calculi. These observations have been confirmed by Fujimaki[24], and recently McCarrison[25] has investigated the problem of the occurrence of urinary calculi in animals and has shown again that they form frequently following inadequate diets. If one may judge from the literature, very little attention has been paid to the possibility that diet may play a rôle in the production of urinary calculi in man, although leukoplakia of the genito-urinary tract has been studied from this viewpoint. Inasmuch as bladder stones are common in sections of the world where deficiency disorders are common, it is a subject worthy of further investigation.

Other conditions, such as xerostomia, may result from changes in the parotid glands due to lack of vitamin A. Changes in the lachrymal glands with diminished or absent lachrymation as a result of vitamin A deficiency are also recognized. In reporting a case of xerostomia and lack of tear secretion, Chamberlin[26] suggested that the changes producing the clinical picture were probably due to a deficiency disorder.

Acrodynia, a comparatively infrequent disease in childhood, occurs most commonly in the second year of life. It is characterized by erythema of the hands, feet and face; particularly of the cheeks and nose, with desquamation of the palms and soles, excessive sweating, alopecia, irritability, insomnia, anorexia, and peripheral neuritis. It has been attributed to a food deficiency by Findlay and Stern[27]. They reported changes in the skin and nervous system of rats which were interpreted as analogous to acrodynia in man. Their results were obtained by feeding autoclaved egg white. Wood[28] is of the opinion that most cases of acrodynia are atypical forms of pellagra and since most patients recover following a good diet, the evidence that it is due to a food deficiency is convincing.

THE RELATIONSHIP OF DEFICIENCY DISORDERS TO ANEMIA

Besides pernicious anemia, which is now considered to be due to a deficiency disorder which develops in most instances as a result of disordered gastric function (Castle[29]), or when there is a pathologic process interfering with normal nutrition[30], there are other varieties of anemia in which the evidence that they are due to a deficiency of substances necessary for blood formation is convincing. If anemia results from a lack of certain substances in the diet, then one would expect it to appear under the same circumstances as other food deficiency syndromes. This is precisely the case. For example, Keefer and Yang[31] have observed anemia in all of the deficiency diseases and Mettier, Minot and Townsend[32] have recently shown conclusively that the anemia associated with scurvy can be due to a lack of vitamin C.

Anemia is also observed in patients with chronic dysentery and results from a restricted diet and the chronic diarrhea[31]. It also is seen in chronic diarrhea due to other causes such as in sprue, tuberculosis of the intestines[33], malabsorption of fat[34, 35, 36], celiac disease[37]. Nutritional factors are also important in other anemias, such as those associated with hookworm

disease[38] or pregnancy. It is clear, then, that anemia is observed under the same circumstances as proved deficiency disorders and in many such cases recovery is observed following diets containing adequate amounts of materials known to stimulate hemoglobin regeneration. Table III contains a list of conditions in which malnutrition may be regarded as responsible for an anemia.

TABLE III

CONDITIONS IN WHICH MALNUTRITION IS A FACTOR IN THE PRODUCTION OF ANEMIA

(1) Inadequate diets, avitaminoses
(2) Chronic dysentery
(3) Hookworm infestation
(4) Pregnancy
(5) Tuberculosis of the intestines
(6) Sprue
(7) Celiac disease
(8) Malabsorption of fat
(9) Partial and complete gastrectomy
(10) Multiple intestinal strictures

IMPORTANCE OF TISSUE CHANGES RESULTING FROM DEFICIENCY DISEASES IN PREDISPOSING TO INFECTION

It is now generally admitted that the tissue changes resulting from food deficiency, and particularly a lack of vitamin A, often predispose patients to infections. These infections have been observed especially in the experimental animal, and it is likely that these experiments have an important bearing on problems concerning infection in children and adults. For example, keratomalacia is frequently associated with infection of the eyelids with blepharitis, meibomitis, and hordeolum, and hyperkeratosis follicularis may progress so that infection occurs about the lesions, and pustules and ulcers of the skin appear. Bronchopneumonia, which is so common in the experimental animal, is also frequently seen in patients with vitamin A deficiency and the fatal case recorded by Wilson and Dubois[39] showed that there was a hyperplasia of the bronchial epithelium to such an extent that the smaller bronchioles were actually occluded in some areas. With the appearance of such changes in the epithelium it is not surprising to find that infection is common under these circumstances.

Of further interest are the lesions of the intestinal tract. Tilden and Miller[40] have shown recently that monkeys fed on a vitamin A deficient diet often develop an ulcerative colitis and they interpret their findings as due to an infection superimposed on the changed intestinal tract. The occurrence of dysentery in patients with vitamin A deficiency is well recognized, and Pillat[19] has described patients with vitamin A deficiency and diarrhea, in whom the diarrhea disappeared with recovery from the deficiency. In his cases bacillary dysentery was excluded by careful bacteriologic examination of the stools. Diarrhea and ulcerative colitis, not due to dysentery, has been described as a complication of edema disease[41] and other deficiency diseases such as pellagra.

It has been reported by McCarrison[42] that monkeys infected with amebic cysts continue to carry them without developing active amebic dysentery until they are given an inadequate diet. Following this procedure, active dysentery appeared.

Peridental infection and dental caries have also been attributed to dietary deficiencies and the question has been studied especially by Mellanby[43] and reviewed recently by Hanke[44]. Mellanby is of the opinion that vitamin A deficiency predisposes to peridental infection, whereas Hanke feels that a lack of vitamin C is also important.

It is seen, then, that deficiency disorders predispose patients to infections as a result of tissue changes, and as these changes may be widespread and affect all epithelial tissue, the manifestations of infection may likewise be extensive.

In cases of deficiency disorders, I have observed obscure pyrexia, arthritis, phlebitis, ulcerative colitis, bronchopneumonia, and pyodermia. The precise relationship between all of these various infections and deficiency disorders is not clear, and further investigation in this field is necessary before final conclusions can be drawn. It is essential, however, in studying obscure infections to appreciate that they may develop in tissues made susceptible by changes resulting from food deficiencies.

From the foregoing discussion it is evident that the clinical manifestations of the deficiency of food substances are variable and widespread. It also is obvious that the clinical picture may be complicated by intercurrent infections and from the previous discussion of the nature of the diets causing deficiencies, the composite clinical picture may be the result of several deficiencies. This may seem platitudinous, but like many other platitudes, it is forgotten in the concrete instance. The outstanding symptoms of a deficiency disease may be so striking that the other features of the clinical picture fade into the background and are not fully appreciated, or, if they are, there is the temptation to account for all of the features on a basis of a single cause. It seems important, therefore, to collect concrete examples of multiple deficiency defects in man in order to emphasize both their occurrence and significance in the interpretation of the clinical picture of deficiency disease.

There is given in Table IV a list of the cases of multiple deficiency defects recorded in the literature together with a number of personally observed cases. From this table it is obvious that one may get various combinations of deficiency disorders in the same individual, and this explains the complexity of the clinical pic-

ture frequently observed. It further emphasizes the fact that if complete recovery from all of the nutritional defects is to be expected, a diet must be supplied which contains in optimal quantities all of the essential food substances.

TABLE IV

CASES OF MULTIPLE DEFICIENCY DISORDERS IN ADULTS

(1) Keratomalacia and Beriberi[3]
(2) Keratomalacia and Rickets[52]
(3) Keratomalacia, Rickets and Beriberi[52]
(4) Keratomalacia and Edema Disease[52]
(5) Keratomalacia and Hyperkeratosis Follicularis[19 37]
(6) Hyperkeratosis Follicularis and Edema Disease[45]
(7) Hyperkeratosis Follicularis and Scurvy[5 46]
(8) Beriberi and Pellagra[47 45]
(9) Beriberi and Scurvy[48 49 50 51]
(10) Beriberi and Rickets[52]
(11) Beriberi and Edema Disease
(12) Hemeralopia and Keratomalacia[10]
(13) Hemeralopia and Beriberi[3]
(14) Hemeralopia and Scurvy[5]
(15) Hemeralopia and Edema Disease[4 45 53]
(16) Scurvy and Edema Disease[5 45]
(17) Rickets and Tetany
(18) Rickets and Edema Disease[52]
(19) Osteomalacia and Tetany[55]
(20) Tetany and Edema Disease[54]
(21) Pernicious Anemia and Scurvy[1]
(22) Pernicious Anemia and Pellagra[1 45]
(23) Pernicious Anemia and Edema Disease and Osteoporosis[35]
(24) Pellagra and Subacute Combined Sclerosis
(25) Pellagra, osteomalacia and tetany[56]

SUMMARY AND CONCLUSIONS

The clinical aspects of food deficiency disorders in man are presented. It is evident that these conditions are observed not only following restricted diets, but also when pathologic processes interfere with nutrition. Multiple dietary deficiency disorders often occur in the same patient and an appreciation of this fact is necessary in order to establish adequate treatment. Deficiency diseases often predispose the patients to secondary infections.

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THE AWARD OF THE LESLIE DANA MEDAL

The Leslie Dana Gold Medal, which is awarded annually for "outstanding achievements in the prevention of blindness and the conservation of vision," was presented in St. Louis, Missouri, November 20, to Edward M. Van Cleve, of New York City, principal of the New York Institute for the Education of the Blind. Mr. Van Cleve was selected for this honor by the National Society for the Prevention of Blindness in coöperation with the St. Louis Society for the Blind, through which the medal is offered by Leslie Dana, of St. Louis.

Mr. Van Cleve played a leading part in the formation in 1915 of the National Society for the Prevention of Blindness, sponsored by the Russell Sage Foundation, and he became its first managing director. After his resignation from this position nine years later, he continued his active interest as a member of the Executive Committee.

The National Society was represented at the presentation by a member of its Board of Directors, Rev. Alphonse M. Schwitalla, S.J., dean of the St. Louis University School of Medicine. Father Schwitalla read a message from Lewis H. Carris, managing director of the National Society, as follows:

"Mr. Van Cleve's nomination for the Leslie Dana Medal met with the greatest enthusiasm on the part of those who have been most familiar with the pioneer work which he did in the first years of organizing the lay movement for the conservation of vision. I regret exceedingly that I cannot be present on this auspicious occasion. It was due entirely to Mr. Van Cleve's great foresight that the National Society adopted a financial policy which has resulted in the wide expansion of its work. Mr. Van Cleve was also very active in extending the Society's coöperation with educational and health agencies throughout the country."

The Leslie Dana Medal was awarded last year to Dr. George E. de Schweinitz, of Philadelphia, former President of the American Medical Association, of the American Ophthalmological Society, and the College of Physicians of Philadelphia. In 1929 the medal was awarded to the late Dr. Ernest Fuchs, of Vienna, Austria, who was recognized in his profession, for a number of years before his death, as "the world's greatest ophthalmologist".

STATE CONFERENCES ON CHILD HEALTH AND PROTECTION

The states are beginning to take up the torch flung to them by The White House Conference on Child Health and Protection which held its final meeting in April. By December 1, fourteen states will already have held their own conferences to take stock of their activities for children and to determine how the findings of the general conference can be put to work in State and community programs. These states are Indiana, Georgia, Utah, New Jersey, New Hampshire, Florida, Mississippi, Maine, Oklahoma, Louisiana, Michigan, Massachusetts, Virginia and Idaho. Four other states, South Carolina, Montana, Ohio and Oregon, have conferences scheduled for the early part of 1932, and several others are working on similar plans. The city of Chicago held a regional conference in October, sponsored by 90 different organizations and attended by 2,000 persons.

Other organizations centering activities about the Children's Charter, according to the *United States Daily*, are: The American Legion, Child Welfare Division; American Library Association, American Child Health Association, American Dental Association, American Association of University Women, Methodist Episcopal Church, South; Kiwanis, National Grange, National Council of Parent Education, National Education Association, American Home Economics Association, Child Welfare League of America, Boy Scouts, Women's Christian Temperance Union, Women of Mooseheart Legion.

The publications of the Conference, embodying the findings of the committees, will total possibly 40 volumes, making, when finished, a comprehensive library of child life. Seven volumes have already appeared: One, "White House Conference. 1930," gives a summary of the main Conference, with the speeches and abstracts of committee reports; three are in the field of education; two in the field of medical care; one in the field of public health.

The Conference maintains an administrative and editorial office in the Interior Building, Washington, D. C., which will continue until the publications have been completed and the follow-up throughout the country initiated. The findings of the Conference will then become an integral part of the State and community programs for the children of the Nation.

THE NEW HAMPSHIRE MEDICAL SOCIETY

SOME TYPES OF "PRIMARY" ANEMIA AND THEIR TREATMENT*

BY WILLIAM DAMESHEK, M.D.†

THE development of marked anemia without apparent cause in a previously healthy individual has always excited interest. Anemia due to various factors such as loss of blood, infection, toxic chemicals or cancer is readily understandable. Here, since the anemia is secondary to a known cause, it is called "secondary anemia". Interest is not usually greatly excited since the etiology is usually readily discernible. There are instances of anemia, however, in which the cause remains wholly obscure, and it is customary, in our ignorance, to call them examples of "idiopathic" or "essential" or "primary" anemia. These cases, because of their unknown origin invite investigation. Certain of them will be discussed in this paper.

FIGURE 1. Photomicrograph of normal bone marrow (autopsy specimen) from rib (× 210). The open areas are fat cells. The cells with black-appearing nuclei are nucleated red cells: normoblasts. The lighter-appearing cells are granulocytes (myelocytes, metamyelocytes, and mature polymorphonuclears).

Before discussing the four illustrative cases, it is necessary to consider the blood cells and their origin. The cells that one counts with the hemacytometer and sees in a blood smear do not originate *de novo* in the bloodstream. They come into it from several sources, and are carried about in the circulating blood to various parts of the body. Most of the blood cells originate in the red bone-marrow of the flat bones, i.e., the ribs, skull, sternum, and parts of the hip bone. Blood circulates sluggishly through the marrow spaces, and in these sinusoids blood formation constantly goes on.

There are three types of formed elements produced in the normal marrow: the red blood cells, the white blood cells, and the blood platelets. The red blood cells and the blood platelets are derived from no other source, but about 25% of the white blood cells owe their origin to sources other than the bone-marrow. In the normal marrow there are islands of active red blood cell formation consisting almost entirely of normoblasts admixed with a few more primitive cells called erythroblasts. The primitive nucleated red blood cell of the fetus known as the megaloblast is not seen. As the cells gradually multiply and ripen, the more mature red blood cells, which stain bluish-gray with Wright's stain and which show a reticulum with the "vital" dye brilliant cresyl blue (reticulocytes) appear in the bloodstream, but their proportion is low, about 0.2-0.5%. White blood cells are also seen in large groups in the bone-marrow. All of this group of cells, except the primitive myeloblast, contain granules. Maturation of the white blood cells in the marrow is orderly, being characterized chiefly by indentation and later polymorphous variation of the nuclei. Occasional amorphous masses constituting the giant cells of the marrow (megakaryocytes) are seen. These in all probability produce the blood platelets.

When the bone-marrow becomes involved by disease, red blood cell formation is interfered with and anemia develops. With failure of proper growth of the bone-marrow red cells (dysplasia) the white blood cells and blood platelets also become reduced in number; the same holds true for lack of growth (aplasia) and for interference with growth by the invasion of foreign cells. On the other hand, there are certain intrinsic disorders of the bone-marrow in which single cell types alone are picked out. Thus, in agranulocytosis, the white cells alone appear to be affected and in purpura hemorrhagica only the megakaryocytes are reduced.

This short review is essential to a proper understanding of the group of cases which will be presented in order to show that anemia is in itself not a diagnosis but rather a manifestation of some underlying pathological process in the bone-marrow.

CASE I—*Pernicious Anemia.*

Isaac A. (Hospital No. 2490), a seventy-year old Jewish cigar sorter was admitted to the Beth Israel Hospital on May 20, 1929, complaining of palpita-

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tion of the heart upon slight exertion. Ten years previously a carcinoma of the rectum had been successfully removed at another hospital; since then he had had a well-functioning colostomy opening. He continued at his work until six months before admission when he noticed precordial pain on slight exertion, palpitation, and increasing dyspnea. Marked tingling and numbness of the finger-tips interfered with his cigar-sorting. Gradual increase in intensity of these symptoms, associated with increasing weakness and anorexia, led him to seek medical advice. He considered himself no paler than he had always been. He had lost about twenty pounds in weight. Physical examination on admission disclosed an undernourished elderly man with marked lemon-yellow pallor. There was definite icterus of the sclerae. The tongue was smooth, atrophied, and reddened at the edges. The heart and lungs were normal. Neither liver nor spleen was palpable. A functioning colostomy wound was present. The

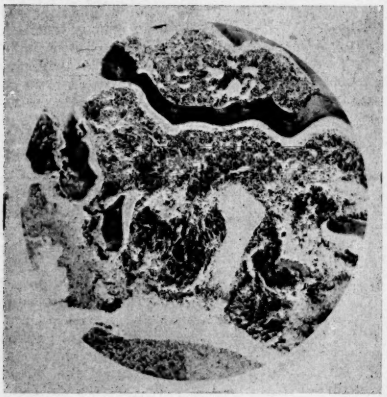

FIGURE 2. Photomicrograph of bone marrow from biopsy of sternum in Case I—pernicious anemia (× 45). The almost complete absence of fat cells and the marked hyperplasia of cells is noted.

reflexes were normal and there was no loss in vibratory sense.

The development of anemia and loss in weight in a man who had had carcinoma of the rectum suggested the diagnosis of carcinomatosis. The symptoms of palpitation, dyspnea, and precordial pain made one suspect myocardial failure and possibly coronary sclerosis. The laboratory data compelled the abandonment of these diagnoses. Several specimens of urines and stools were normal. Gastro-intestinal series showed nothing beyond a well-functioning colostomy. X-ray of the chest taken at a distance of seven feet was negative. The electrocardiogram was not unusual. Gastric analysis disclosed complete absence of free hydrochloric acid. The icteric index was 11; bilirubin 1.5 mg. per 100 cc. Hemoglobin (Sahli) was 37%; red blood cell count 1.63 millions; white blood cell count 11,900; reticulocytes 0.8%; blood platelets 340,000 per cu. mm. The red blood cells were without achromia; there was marked variation in size and shape of the cells; they varied in diameter from 3 to 12 micra, the average being 8.37 micra. Fifty-five per cent. of the cells were 9 micra or over. No nucleated red

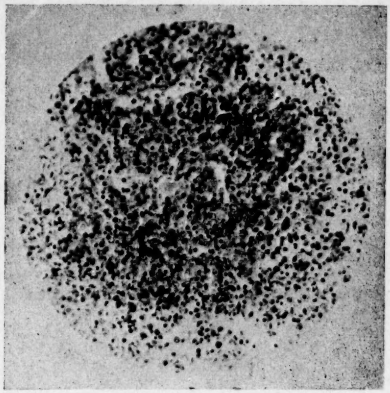

FIGURE 3. High power of Figure 2 (× 240). Island consisting almost entirely of large primitive nucleated red cells: megaloblasts. Intermingled are the smaller normoblasts with pyknotic nuclei.

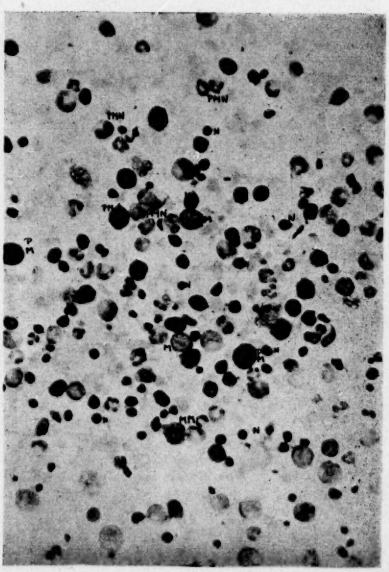

FIGURE 4. Photomicrograph of bone marrow smear made from biopsy of sternum in Case I—pernicious anemia (× 380). Special Wright's stain. The large dark-staining cells are pro-megaloblasts (PM). At "M" more mature megaloblasts. At "MM" is a megaloblast in mitosis. Numerous normoblasts (N), myelocytes, metamyelocytes, and mature granulocytes (PMN) are seen.

blood cells were seen. Differential count of the white blood cells showed: neutrophiles 23.5%; lymphocytes 75.5%; monocytes 0.5%; eosinophiles 0.5%. The lack of achromia, the large size of most of the red blood cells (macrocytes), the diminished blood platelet count (normal 600,000-800,000 by the method used) and the low polymorphonuclear count were all typical of the blood picture of pernicious anemia. The slight increase in leukocyte count which was due to a marked increase in lymphocytes could not be explained but was thought to be associated in some way with the colostomy wound. In order to remove any doubt as to the diagnosis, a biopsy of the sternal bone marrow was done. This showed an exceedingly hyperplastic marrow which contained large numbers of embryonic nucleated red blood cells, i.e., megaloblasts. The ratio of red cells to white cells, normally about 1:1, was 4.5:1.

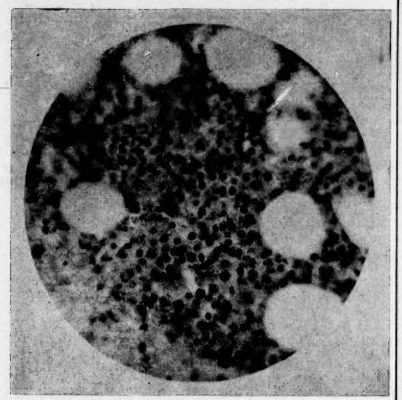

FIGURE 5. Photomicrograph of bone marrow from biopsy of sternum in Case I after treatment with liver extract (× 520). Numerous normoblasts instead of the former megaloblasts are seen.

97.7% of the red cells were definitely embryonic, only 1.3% being the more mature normoblastic cells. The megaloblasts were present in large islands and frequent mitotic figures were seen in them.

There was now no doubt of the diagnosis. The bone-marrow which was hyperplastic despite the marked anemia and which contained large numbers of megaloblasts was pathognomonic of pernicious anemia. The patient was accordingly placed on liver extract and whole liver. There was prompt increase in the number of reticulocytes and red cells in the blood so that in less than four weeks the hemoglobin had risen to 70% (Sahli) and the red blood cell count to 3.65 millions. The blood smear showed now slight achromia and much less variation in size of the individual red blood cells. The average red blood cell diameter was now practically normal: 7.6 micra and only 23% of the cells were 9 micra in diameter, no larger cells being seen. A second bone-marrow biopsy was done at this time and showed instead of a megaloblastosis a proliferation of normoblasts, with rare megaloblasts. This is in accordance with the observations of Peabody[1], who found the same reversion to a more normal type of marrow in pernicious anemia after liver treatment. There was gradual improvement in the blood picture so that by March 1930 hemoglobin (Sahli) was 76% and erythrocyte count 5,000,000 per cu. mm.

DISCUSSION

There are a few points in this patient's history which should be stressed. The appearance of pernicious anemia in elderly individuals is the rule rather than the exception. Again, marked loss in weight is a common finding in this disease despite the general belief that pernicious anemia occurs in well-nourished individuals. It should be noted that this patient has already escaped two supposedly fatal diseases: carcinoma and pernicious anemia. The colostomy opening and the abnormal intestinal function which has probably resulted, brings up the very interesting question as to the rôle of the gastro-intestinal tract in the etiology of this disease. Several authors have discussed the relationship of intestinal lesions to pernicious anemia[2], and to the development of pernicious-anemia-like blood pictures. Thus, in sprue[3] and in certain cases of bacillary dysentery[4] a blood picture indistinguishable from that of pernicious anemia is frequently seen. Some defect of the intestinal tract may allow, according to other authors, the profuse growth of Bacillus Welchii, and the absorption of the toxin produced is supposed to cause the disease[5].

Castle[6] has shown in a convincing array of experiments that the gastric secretion of a patient with pernicious anemia is unable to digest protein adequately. An unknown factor, probably an enzyme, is lacking. If gastric juice removed from a normal human is incubated with meat and the resulting digestion mixture fed to a patient with pernicious anemia, a response as great as is obtained with liver will result. The gastric juice of a patient with pernicious anemia appears to be devoid of some unidentified factor, important in the proper digestion of protein. Without this digestion bone-marrow growth cannot proceed in an orderly fashion. The megaloblasts are "frozen"—there is inadequate or abnormal growth (dysplasia)—and anemia develops. Given normal gastric juice incubated with meat[6] or a peculiar protein which apparently does not require this digestion (liver)[7] or whole dried hog's stomach which appears to contain both the unidentified factor and the protein substratum[8] the megaloblasts proceed in an orderly fashion to rapid maturation, and the bone-marrow becomes normoblastic. In the peripheral blood we see first a rapid increase in the number of reticulocytes which is followed by a gradual and sustained rise in the red blood cell count. Why certain adult individuals should have megaloblasts in their marrow and others not is not known. This brings up the very interesting hereditary or constitutional factor in pernicious anemia, which for lack of space will not be discussed here.

CASE II*—*Primary Hypochromic Anemia.*

Helen H. (hospital No. 7142), a married housewife of forty-four, a native of Canada who had lived in New England for four years, was admitted to the Beth Israel Hospital on July 1, 1930, complaining of pallor and dyspnea. She had had numerous diseases in the past, none of which appeared to be relevant to the present illness. This began about five years before admission, when she became markedly pale, weak, dyspneic, and had severe diarrhea. She lost thirty to forty pounds in weight. A diagnosis of "anemia" was made and treatment with "iron pills" instituted. Her color and strength gradually returned and she gained twenty pounds in weight. However, one year later (three years before admission) the same symptoms recurred and were relieved by the same "iron pills". A third recurrence of the identical symptoms appeared two years before admission. The patient did not consult a doctor nor take any iron. The symptoms became progressively worse. A year and a half before admission she developed menorrhagia and at times metrorrhagia. In December 1929, six months before admission, her tongue became markedly sore so that she was unable to eat oranges or any other "acid" fruits or vegetables. This was soon followed by numbness and tingling of the fingers and tongue. Finally, she could hardly drag herself about and was dyspneic even on walking across the floor. She first came to the Boston Dispensary in June 1930 and was referred to the Beth Israel Hospital for study. At no time had she taken any drugs other than those mentioned above. Her appetite was extremely poor but she had eaten meat, green vegetables, and fruits in moderate amounts.

Physical examination on admission showed a thin woman with extreme pallor. There was no icterus of the sclerae. The tongue was smooth, atrophied and without coat; there was some redness at the edges. A soft systolic murmur was heard over the precordium. The liver edge was barely palpable; the spleen was not palpable. The left knee jerk was present, though sluggish; the right absent. A positive Babinski response was present on the left and absent on the right. Vibratory sensation was undisturbed. The uterus was slightly enlarged. Blood pressure was 115 systolic; 50 diastolic. Temperature was 99.8 degrees Fahrenheit.

Laboratory examinations were as follows: Wassermann, Kahn, and Hinton tests negative; gastrointestinal x-ray series negative except for questionable adhesions in the right lower quadrant of the abdomen; barium enema negative; plain plates of the kidneys, ureters, and bladder negative; cholecystograms by the dye method negative; x-rays of all the long bones, vertebrae, skull, and chest negative. A large number of urine specimens were normal; four stools showed no occult blood. Icteric index was four. Gastric analysis with 7% alcohol test meal followed in forty-five minutes by intramuscular injection of 0.5 mg. of histamine showed no free hydrochloric acid one hour after histamine was given and a total acidity of four at the same period; the volumes of gastric juice obtained were exceedingly low. Blood studies showed the following: Hemoglobin 20% (Dare and Sahli); red blood cell count 2.7 and 2.3 million per cu. mm.; white blood cell count 3700 and 4050 per cu. mm.; polymorphonuclears 45%; lymphocytes 51%; monocytes 0; eosinophiles 4%; basophiles 0. Red blood cells showed very marked achromia, extreme change in size and shape with small cells predominating and little or no polychromatophilia. Average red blood cell diameter was 6.02 micra, the cells varying from 3 to 7 micra. The blood platelet count was 267,000 per cu. mm. by an indirect method (normal 500,000 per cu. mm.) Reticulocytes numbered 0.7%.

This patient therefore had the typical symptomatology of pernicious anemia, namely: Marked anemia, diarrhea, burning tongue, weakness, dyspnea, all showing remissions and relapses; and finally numbness and tingling of the finger-tips and difficulty in walking. The physical examination, too, except for the lack of icterus, was consistent with pernicious anemia in that the tongue was atrophied, and signs of combined system disease were present. The blood findings, however, were typical of what is ordinarily called "secondary anemia",

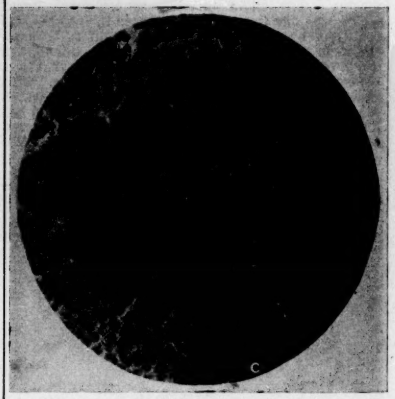

FIGURE 6. Photomicrograph of bone marrow from biopsy of sternum in Case II—primary hypochromic anemia (× 500). Note the marked cellular hyperplasia despite the severe anemia and leukopenia.

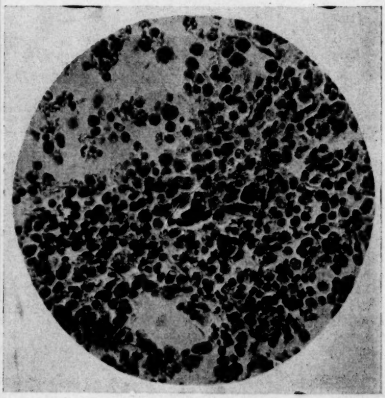

FIGURE 7. High-power (× 800) of bone marrow biopsy of Case II. The cells with pyknotic nuclei are normoblasts, the larger cells with prominent masses of chromatin in their nuclei being erythroblasts.

*This case is No. 1 in a paper on "Primary Hypochromic Anemia", *American Journal Medical Sciences*, 182:520 (Oct.) 1931.

that is, there was a low color index, achromia, small red blood cells and a low average red blood cell diameter. This seemed to be then a case of pernicious anemia from the clinical standpoint but of secondary anemia from the hematologic standpoint.

A biopsy of the sternal bone-marrow performed on July 10 showed an exceedingly hyperplastic marrow, crowded with large numbers of nucleated red cells, frequently in large "islands". These islands contained chiefly erythroblasts although numerous transitions between these cells and typical normoblasts were seen. No megaloblasts were found.

As we have seen, the bone marrow in pernicious anemia, despite the marked anemia, is hyperplastic and crowded with immature embryonic red cells (megaloblasts). In this patient, also, despite the severe anemia, the bone marrow was hyperplastic and showed large numbers of immature red blood cells, which, however, were normal or adult cells: i.e., erythroblasts. This difference could account for the variation in the blood picture in the two cases: in pernicious anemia the extremely large megaloblasts produce large red blood cells called macrocytes; in the case under discussion here, the smaller erythroblasts produced small red blood cells called microcytes.

CLINICAL COURSE

On admission, the patient was given a four thousand calorie diet of which she ate only about one-half, and continued to lose weight. For ten days she was regularly given four vials of liver extract daily (Lilly No. 343) but without clinical or hematological improvement. In fact, the anemia became slightly more severe during this period. On July 21, she left the hospital against advice. However, on discharge, she was advised to take ferric and ammonium citrate in doses of one gram three times daily (in 25% aqueous solution), and to continue with her regular diet. On July 21, the day of discharge, hemoglobin was 15%, red blood cell count 1,960,000 per cu. mm.; white blood cell count 5100 per cu. mm. She returned to the Blood Clinic nine days after discharge. She had felt no change for three days. However, on the fourth day after starting the iron therapy, she awoke feeling a great deal better, and very hungry. She then began to eat ravenously and continued to do so. Her tongue became less sore and the numbness and tingling of the fingers were diminished. During this nine-day period, hemoglobin had risen from 15% to 35% and the red blood cell count from about 2,000,000 to about 3,000,000 per cu. mm. The reticulocytes were increased to 6.7%, but possibly the peak of the reticulocyte increase had been passed. Polymorphonuclears and platelets also showed a definite increase in numbers. However, during the next few days, there was a slight diminution in the numbers of leukocytes and platelets and the dosage of ferric and ammonium citrate was therefore doubled to six grams daily. In another week there was another marked response, so that on August 9, hemoglobin was 46% and erythrocyte count 3,950,000 per cu. mm. The number of blood platelets had reached the astonishing level of 1,200,000 per cu. mm. and reticulocytes numbered 9.6%. Her tongue bothered her no longer; she could now tolerate even vinegar. There were now no paresthesias. Appetite continued to be ravenous so that she ate almost constantly. There was no weakness or dyspnea. The patient was gaining considerable weight, and her color was now quite pink. She said that she felt better than for many years. From that time on there was continued clinical and hematologic improvement. On October 29, three months after iron therapy was started, hemoglobin was 88%; red blood cell count 4,640,000 per cu. mm.; white blood cell count 6500 per cu. mm.; blood platelet count 600,000 per cu. mm.; reticulocytes 0%. She had voluntarily discontinued iron therapy about a month previously. There was remarkable clinical improvement. Her face was extremely red, almost plethoric. She was now quite robust, her weight being 158 pounds. She has since failed to return to the clinic.

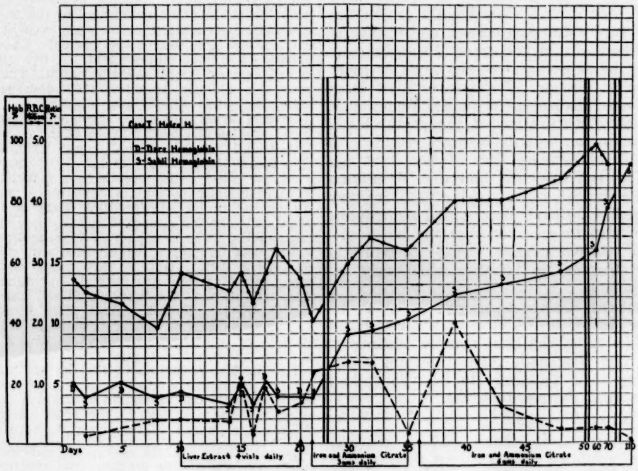

FIGURE 8. Primary hypochromic anemia. Effect of treatment with large doses of iron.

DISCUSSION

This patient, then, had all the typical symptoms of pernicious anemia, and most of the signs of that disease. The blood picture, however, was that of "secondary anemia" and the bone marrow was crowded with erythroblasts instead of with the embryonic megaloblasts found in pernicious anemia. There was no response to liver extract but striking response to large doses of iron.

This condition might be considered as an unusual type of pernicious anemia associated with an erythroblastic rather than a megaloblastic bone marrow. Recently twelve patients with a very similar clinical syndrome have been observed. I have proposed for this syndrome the term "primary hypochromic anemia"[9] since the disease is evidently primary or idiopathic in nature and is associated with hypochromia of the red cells. It is probable that the anemia, as in the classical Addisonian anemia is dependent upon a type of defective maturation of the red blood cells in the marrow. By analogy with "pernicious anemia" in which there is also no hydrochloric acid in the stomach, the underlying defect may be some gastric disturbance. This, in turn, may lead to an inadequate digestion of organic iron, thus permitting (to paraphrase Castle[6]) the development of a virtual iron deficiency in the presence of a normal diet. These patients respond remarkably well to large doses of inorganic iron but, as with liver therapy in pernicious anemia, the dose must be adequate. For this reason, total daily doses of six to eight grams of a soluble iron preparation (ferric and ammonium citrate) in aqueous solution have been given. Occasionally gastric distress and rarely diarrhea ensues, and if this occurs, reduced iron in one gram (15 grain) capsules may be substituted in the same or somewhat smaller dosage. Response to these large doses of iron medication is indeed remarkable. The defective maturation of the erythroblasts in the marrow apparently becomes rectified for there is an outpouring first of immature red blood cells (reticulocytes) and then of mature red blood cells with accompanying rapid increase in hemoglobin. Blood platelet and neutrophile formation also increase, so that the blood picture soon becomes normal. There is typically a marked increase in appetite which may become voracious.

This patient illustrates another type of disturbed or faulty mechanism in the red blood cell production in the bone marrow leading to anemia. This dysplastic type of anemia is due presumably to a deficiency in iron dependent upon disturbed gastric digestion.

CASE III—*Aplastic Anemia.*

Edna S. (Hospital No. 8312), a twenty-five year old housewife entered the Beth Israel Hospital September 30, 1930 complaining of weakness of two months' duration*. Until the present illness she had always been well. On February 26, 1930 she had come to the Outpatient Department where she presented the typical lesions of lupus erythematosus on the face. These had been present since December 1929, and were apparently spreading. She was given a series of nineteen weekly intravenous injections of gold sodium thiosulphate. The first injection—0.050 g.—was followed by slight transitory stiffness about the left knee, not associated with any other symptoms. The second injection was accordingly reduced to 0.025 g., the third was 0.050 g., the fourth 0.075 g., the fifth and all subsequent injections consisted of 0.100 g.

On April 9, 1930 because of persistent pain in the right shoulder and left arm, a complete physical examination was made but nothing abnormal was found. At this time the hemoglobin (Tallqvist) was 70%. The stained smear showed slight aniso-and poikilocytosis of the red blood cells, and a normal differential count of the white blood cells (neutrophiles 65%, lymphocytes 22%, monocytes 11%, eosinophiles 1%). X-rays of the teeth showed areas of absorption and diminished density below the roots of three teeth. These teeth were extracted. The skin lesions were showing improvement and the injections were continued. About this time the skin over the hands and forearms presented an itchy rash, became rough and scaly, and finally desquamated. The lesions of lupus erythematosus had finally entirely disappeared by August 6, 1930 and the injections of gold sodium thiosulphate were therefore discontinued.

However, starting at about the time of cessation of the injections, there developed dyspnea, palpitation, severe headache and rapidly progressing pallor and weakness. Slight trauma caused large ecchymotic spots on the patient's legs and arms and there was marked increase in menstrual bleeding. Progressive increase of these symptoms during the next two months finally led to hospitalization on September 30, 1930.

Examination on admission disclosed a well-developed and nourished but very pale woman without icterus. Two small pinpoint petechial spots were noted on the mucous membrane of the hard palate, and fading ecchymotic areas were present over the extremities. The tongue was normal. There was no hepatic or splenic enlargement. A few slightly enlarged, cervical lymph-nodes were felt. The temperature was slightly elevated (100 degrees Fahrenheit), the pulse 100-120 per minute.

Several urine and stool specimens were normal. Blood studies disclosed marked anemia: hemoglobin 45% (Sahli); red blood cell count 1,970,000; leukocyte count 3200; blood platelets 10,000 per cu. mm. The red blood cells, despite the marked anemia, were practically normal in appearance, round, and without achromia. Differential count of the white blood cells showed a marked relative lymphocytosis: neutrophiles 16%, lymphocytes 74%, monocytes 5%. There was no polychromatophilia and reticulocyte count was 0.3%. Only a rare blood platelet was seen. Bleeding time was normal, four minutes; clotting time (3 test tube method) fifteen minutes; the clot, however, did not retract after fifteen hours. The fragility test was normal, hemolysis beginning at .40% of sodium chloride and becoming complete at .38%. Icteric index was 6.

The marked reduction in (1) the red blood cells, (2) the polymorphonuclear neutrophiles and (3) the blood platelets was indicative of either a destructive or an aplastic condition of the bone marrow, since all three elements of the marrow were involved.

*It is a pleasure to record here my thanks to Dr. Albert A. Shapira for permission to study this case and for his many courtesies in connection with it.

The normal or slightly elevated color index, the normal size and shape of the red cells and the extreme reduction in blood platelets were consistent with a diagnosis of aplastic anemia. Bone marrow biopsy (sternum) was done and the finding of a completely fatty marrow with but a few tiny islands of blood formation confirmed this diagnosis.

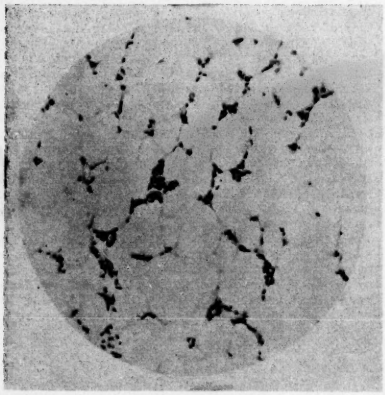

FIGURE 9. Photomicrograph of bone marrow from biopsy of sternum in Case III—aplastic anemia (× 240). Note almost complete replacement of bone-marrow tissue by fat with only few small areas of cell formation.

The anemia rapidly became more marked so that on October 5, 1930 she was given the first transfusion of blood. This resulted in only a temporary alleviation of the symptoms so that it became necessary to give a series at approximately bi-weekly intervals of seventeen transfusions. Each transfusion gave immediate relief and raised the red blood cell count 600-700,000 per cu. mm. However, within two weeks after this measure, the patient would again appear almost exsanguinated, bleeding from various sources, and complaining of marked palpitation of the heart and severe headache. Red blood cell counts at these times showed figures ranging from 1,000,000 to 1,800,000 per cu. mm. It was noted that the symptoms usually reappeared when the red blood cell count fell below 1,900,000 per cu. mm. In spite of the oft-repeated transfusions, the patient gradually grew weaker, developed minor infections of the skin and severe subcutaneous hemorrhages.

She entered the hospital for the last time on April 15, 1931 because of severe abdominal pain with vomiting. Several subconjunctival hemorrhages and a peculiar grayish-yellow pallor to the skin gave her an awesome appearance. Another transfusion was immediately given and was followed by a marked reaction characterized by fever, angioneurotic edema, asthma, and hemoglobinuria. On the following day she was given another transfusion of 500 cc. of blood. Three days later she developed a cough and pain in the left chest. A pleural friction-rub in the left axilla and numerous crepitant râles in the left mid-chest posteriorly were found. She became comatose and died on April 21, 1931. During the nine months after onset of anemia, eight liters of blood had been transfused from numerous donors with no indication of regenerative activity of the bone marrow. The consequent lack of white blood cells led to poor defense against infections. The lack of blood platelets was conducive to numerous hemorrhages. Finally a mild transfusion reaction probably had a great deal to do with the patient's death. Permission for autopsy was not obtained.

DISCUSSION

Although in most cases of aplastic anemia no etiology can be determined, in numerous instances such substances as benzol, arsenic, arsphenamine, the radio-active metals and x-rays have all been established as the cause of bone marrow aplasia[10]. It is possible that eventually the etiology in all cases of aplastic anemia will be found. In the case under discussion it was felt that the long series of intravenous injections of gold sodium thiosulphate might have some etiologic relation to the aplastic anemia. A fairly careful search of the literature failed to reveal any reported cases of aplastic anemia following treatment with sanocrysin, as the above-mentioned chemical is known in Europe. It has been used, particularly in the Scandinavian countries, in the treatment of pulmonary tuberculosis and in this country in the treatment of lupus erythematosus. Although a biopsy of the skin failed to reveal any gold, this did not exclude this metal as an etiologic agent since it had probably been entirely excreted since the last treatment.

CASE IV—*Anemia Due to Aleukemic Reticulo-Endotheliosis.*

Charles M., a thirty-nine year old Italian textile worker, entered the Laconia Hospital, Laconia, New Hampshire on September 25, 1930 complaining of weakness and fever*. He had been a weaver in a woolen mill for a number of years. Born in Italy, he came to this country in 1913. Except for gonorrhea in 1912 and influenza in 1918 he had always considered himself well until August 1930. At that time, he began to feel somewhat weak and noticed that he was feverish at times. He grew gradually weaker and extremely pale and was finally admitted to the hospital for study. Physical examination on admission revealed nothing abnormal except pallor. It was however noted that he had a peculiar relapsing type of fever. The temperature gradually rose during the course of about five days to 102-103 degrees Fahrenheit, remained elevated for five days, and gradually returned to normal during a period of five days, remaining finally at normal for another five-day period. This sequence of events was repeated regularly during the course of the next several months. During the febrile periods the patient became weak, lost his appetite, developed slight gastric distress and marked constipation, and became increasingly pale. During the afebrile periods these symptoms subsided. In the last week of December 1930, gastro-intestinal symptoms became more pronounced and there was increasing abdominal distention, belching, and rectal gas. Except for nocturia, probably dependent upon insomnia, there were no other symptoms. During these three months, there had been a loss of about twenty pounds in weight.

Numerous laboratory tests were performed in an effort to establish a diagnosis. Several urine and

*I am indebted to Drs. Smart and Robinson of Laconia, New Hampshire, for the opportunity of seeing the patient and for the many courtesies which they extended to me.

stool specimens were normal; the Widal reaction was doubtful once, positive once, and negative once; cultures of the stools were negative for typhoid bacilli; agglutination tests for B. melitensis were negative; blood smear showed no malarial parasites; blood Wassermann reaction was negative. Fluoroscopic examination of the chest was negative, as was a gastro-intestinal series. There was a constant leukopenia, the leukocyte count ranging between 3200 and 3500 per cu. mm. On December 4, 1930, hemoglobin (Sahli) was 55%; red blood cell count 2,832,000; white blood cell count 3500. The stained smear showed some change in size and shape of the red blood cells. The differential count of the white blood cells was not abnormal. Treatment, in the absence of a definite diagnosis, was unsatisfactory. Liver extract, ferric citrate, occasional doses of quinine, two injections of neo-arsphenamine were given, all without influence on the symptoms or the progressive anemia.

On January 1, 1931 when I first saw the patient, he was exceedingly pale. The heart and lungs were normal. The liver appeared to be moderately enlarged, its edge being felt two fingerbreadths below the right costal margin. The tip of the spleen was just felt with deep inspiration. One small lymph node, the size of a pea, was felt in the left supraclavicular fossa. No other peripheral lymph nodes were palpable. The hemoglobin was 30% (Sahli); erythrocyte count 1,890,000; leukocyte count 1100; blood platelets 123,000; reticulocytes 1.5%. The red blood cells showed no achromia; there was marked variation in size but only slight variation in shape of the red cells. Average red blood cell diameter was 7.35 micra. Differential count of the white blood cells showed: polymorphonuclears 72.5% (8.5% immature), lymphocytes 9.5%, monocytes 16% (1% histiocytes), eosinophiles 1.5% and unclassified cells 0.5%.

Even at this time, the diagnosis was still obscure, and several possibilities were to be considered. One of these was Hodgkin's disease. Patients with this disease at times present a relapsing fever of the "Pel-Ebstein" type. This type of fever (Fig. 10) was present here. Although there was but one enlarged superficial lymph node, the presence of Hodgkin's disease largely localized in the intestinal tract was to be considered. The increase in gastro-intestinal symptoms in the present case could very well be associated with such a condition. Against Hodgkin's disease, however, was the blood picture. Although anemia may develop in the last stages of the disease, it is seldom severe and is not associated with a marked leukopenia or diminution in blood platelets; in fact the blood platelets are usually increased in number.

Another possibility was aplastic anemia. The marked reduction in erythrocyte count, the leukopenia, the diminution in blood platelets all pointed to an aplastic condition of the bone marrow. However, the lengthy course without bleeding or petechiae would be most unusual in ordinary aplas-

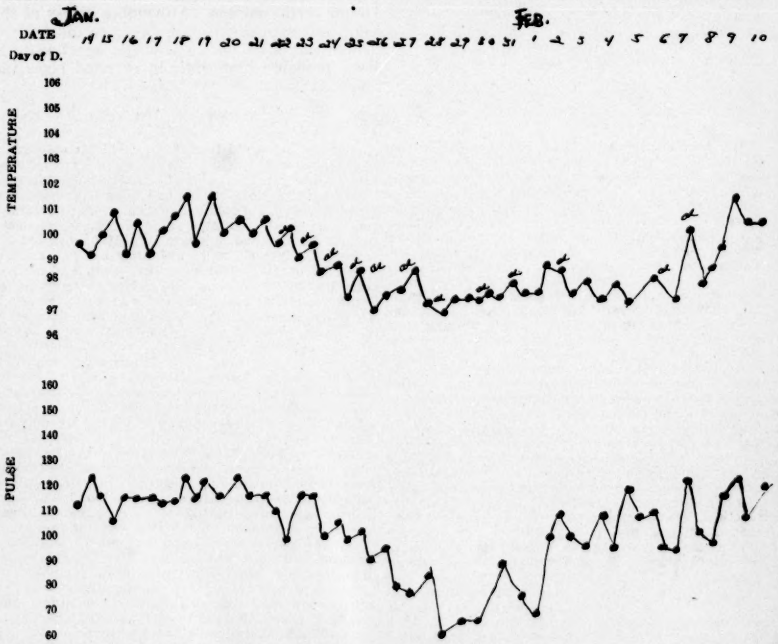

FIGURE 10. Temperature chart of Case IV — aleukemic reticulo-endotheliosis. Note the relapsing type of fever, typical of the "Pel-Ebstein" pyrexia, characteristically seen in the late stages of Hodgkin's disease.

tic anemia. Again, leukemia of the aleukemic type could probably be ruled out because the absence of generalized lymph node enlargement was against the lymphatic type of leukemia and the absence of marked splenic enlargement against the myelogenous type. It was finally concluded that the blood findings could only be due to some destructive process involving most of the bone marrow and interfering with the normal growth of red cells, white cells and megakaryocytes. Ordinary Hodgkin's disease,

FIGURE 11. Photomicrograph of bone marrow from biopsy of sternum in Case IV—aleukemic reticulo-endotheliosis (× 450). Note the replacement of the normal marrow cavity by dense fibrous tissue.

although it may occasionally invade the marrow by direct extension does not cause profound marrow aplasia. Four patients had recently been observed at the Beth Israel Hospital in whom lymphosarcoma by metastasizing widely into the bone marrow brought about a severe aplastic type of anemia. It was felt that an analogous condition might exist in this patient.

Biopsy of the sternal bone marrow was accordingly done. The bone marrow cavity was easily entered, but instead of the soft red spongy material usually found, pearly-white, hard, brittle marrow was encountered. Smears made from this tissue showed masses of fibrous tissue among which were large cells, the identity of which could not be established. Sections disclosed dense fibrous tissue replacing almost completely the normal bone marrow elements. Nucleated red cells and myelocytes were rare. Besides the fibrous tissue, there were collections of large cells with pale vesicular nuclei; these showed no particular arrangement; giant cells and mitotic figures could occasionally be seen. Two pathologists considered the picture consistent with Hodgkin's disease; two others would not commit themselves beyond saying it was some form of tumor which was growing in the marrow with resultant fibrosis.

The patient gradually grew worse. Finally the abdomen became distended and signs referable to an incomplete intestinal obstruction developed. He became comatose and died on February 26, 1931. Drs. Smart and Robinson obtained permission for autopsy and kindly sent some of the organs to us for further examination. Dr. Monroe J. Schlesinger has been kind enough to study the tissues.

The gross findings at the autopsy showed numerous large, very hard lymph nodes which were greyish on cut surface. The liver was firm, mottled and appeared to be replaced in part by firm greyish tissue. The spleen was large and appeared similarly involved. Near the ileocecal junction was a hard tumor mass, arising from the intestinal wall, and causing incomplete obstruction at that point.

On microscopic examination both the spleen and liver showed numerous small areas composed of very large cells with large vesicular nuclei. In these areas multinucleated giant cells as well as large cells with single large "unilocular" nuclei were seen. The lymph nodes disclosed almost complete effacement of the normal architecture. Lymph follicles were nowhere recognizable. Intermingled with the reticulo-endothelial cells forming the sinuses were large numbers of giant cells similar to those found in the liver and spleen. These resembled quite closely the Dorothy Reed type of giant cell found in Hodgkin's disease except that instead of being usually multinucleated, most of the cells were "unilocular giant cells," i.e., they contained a large, twisted, irregular, basket-shaped nucleus ramifying throughout the cell. Many of these nuclei showed one or more prominent nucleoli. Fibrosis of the lymph nodes was not a prominent feature; no

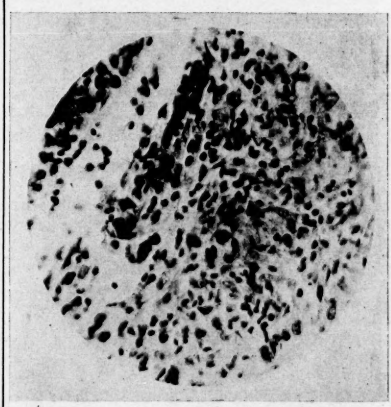

FIGURE 12. High power (× 450) of Figure 11. Note the dense tissue composed of groups of cells growing without particular arrangement. The large, oval, reticulo-endothelial cells with large vesicular nuclei are seen growing in profusion among the sparse normoblasts.

eosinophiles were found; and no mitotic figures were seen. Sections of the bone marrow from a rib disclosed findings almost identical with those discovered at biopsy of the sternal bone marrow in January.

The tumor of the intestines was found after investigation with special stains to be a benign fibroma and not a malignant neoplasm and probably not connected in any way with the more generalized pathological process. The latter condition was finally adjudged to be an extremely rare form of neoplastic process: Reticulo-endotheliosis. This represents a proliferation of the reticulo-endothelial system, which is composed of phagocytic cells (histiocytes) scattered throughout the body, particular-

ly in the spleen, liver, lymph nodes and bone marrow. The monocytes of the blood-stream are in all probability derived from these cells[11]. Abnormal proliferation of this system with the appearance of large numbers of monocytes and histiocytes in the circulating blood has been described under the

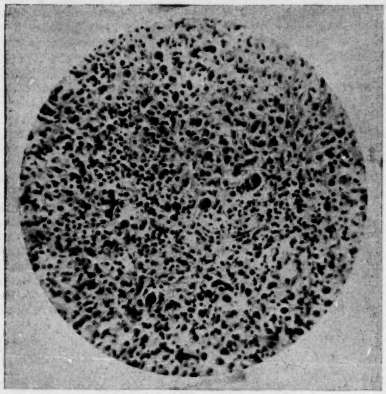

FIGURE 13. Photomicrograph of autopsy specimen of lymph-node of Case IV (× 220). Note complete effacement of the normal lymph-node architecture by the same type of cells present in the bone-marrow. The giant cells very similar to the "Dorothy Reed" cells of Hodgkin's disease are conspicuous.

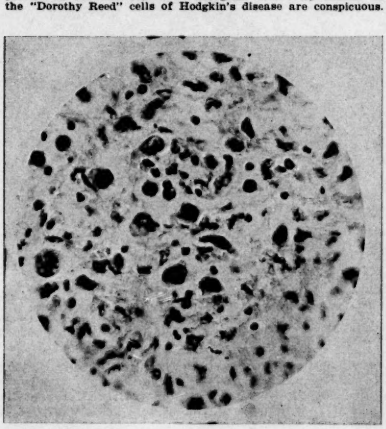

FIGURE 14. High power (× 520) of Figure 13. The type cell is the large reticulo-endothelial cell which is seen growing without orderly arrangement. Numerous "unilocular" giant cells are seen.

names of monocytic leukemia and reticulo-endotheliosis. (Dameshek[12], Schwirtschewskaja[13], Hittmair[13].) Hyperplasia of the same system without the appearance of an increased number of these cells in the blood stream has recently been described abroad by Letterer[14], Goldschmidt[15], and Sachs and Wohlwill[16] as aleukemic reticulo-endotheliosis or the aleukemic form of monocytic leukemia. This condition is thus a proliferative lesion closely allied to Hodgkin's disease which itself is held by many to be a form of reticulo-endotheliosis[17]. It is interesting that the Pel-Ebstein type of relapsing fever, encountered in classical cases of Hodgkin's disease should also occur in this pathologically similar condition.

DISCUSSION

The illustrative cases described demonstrate that not all of the patients with "idiopathic" anemia are suffering from the disease pernicious anemia. It may be true that most of the instances of anemia which arise *per se* are examples of this disease, but one should not forget in the differential diagnosis aplastic anemia, hypochromic anemia, and anemia due to invasion of the marrow by leukemic or a related process. I have stressed the importance of analyzing each individual patient with anemia by trying to find out what is going on "behind the scenes", i.e., in the bone marrow. The blood-stream gives us very important clues to be sure, but does not present the entire picture. We should attempt to understand the mechanism of the production of the anemia not by merely giving it a label or by stating that the blood picture is "secondary" or "primary", but in terms of what is happening in the center of red blood cell formation: the marrow. A study of the bone marrow as obtained from the sternum by biopsy has accordingly been given with each case cited.

It is obvious that treatment without an exact diagnosis tends to be without benefit either to the patient's disease or to the doctor's knowledge. Without proper study, liver and liver extract should not be indiscriminately used in the treatment of any patient with anemia. Such treatment tends to bring about diagnostic slovenliness, and may also make diagnosis more difficult for the next physician. Again, shotgun methods in which a dose of liver is mixed with a dose of iron are frequently used. This practice does not increase our knowledge as to the value of either mode of therapy. Liver extracts of various types have in my experience proved to be of no value in patients with anemias in which a low color index and achromia are present, but their use appears to be reserved rather for the one disease pernicious anemia. The combination of liver extract and iron in these hypochromic anemias appears to be of no greater therapeutic effect than iron alone. Whole liver appears to be of somewhat greater benefit in this connection because of its iron content. The various proprietary mixtures which contain iron, liver, liver extract, bone marrow, blood, etc., are to say the least, unscientific.

Transfusions are less frequently given in the idiopathic anemias since the introduction of liver therapy in pernicious anemia. Even the extremely severe case of this disease in which the

red blood cells are reduced to a figure as low as 800,000 per cu. mm. can be satisfactorily treated by large doses of liver extract. However, as in the case numbered III above (aplastic anemia) multiple transfusions are often used to prolong the patient's life with the forlorn hope that regeneration of the marrow may occur. No other therapy is known for this condition.

In short, the treatment of a patient presenting anemia should whenever possible proceed as an outgrowth of the diagnosis, and the diagnosis should come about as the result of an analysis of the symptoms, the signs, and the laboratory data in addition to an understanding of what is behind the findings in the blood, namely in the bone marrow.

SUMMARY AND CONCLUSIONS

1. Four cases of idiopathic or "primary" anemia are described and discussed. Represented are instances of pernicious anemia, primary hypochromic anemia, aplastic anemia and anemia due to aleukemic reticulo-endotheliosis.

2. The findings in the peripheral blood of the illustrative cases are correlated with those in the bone marrow as obtained from biopsy of the sternum.

3. The treatment of a patient with anemia should be based upon an understanding of the mechanisms involved in the production of the anemia.

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DISCUSSION

DR. RICHARD W. ROBINSON, Laconia: This is a very interesting presentation as it opens to discussion the whole field of the anemias, a subject the complexities of which are so great that the more we consider them the more we find that our knowledge is not entirely adequate to their understanding. I think that there is no such thing as primary anemia, that is, a disease entity, such as chlorosis, or pernicious anemia, which is the sole expression of the disease, an explanation of which is to be found in the blood and the blood-forming organs. It is more than probable that pernicious anemia, for instance, is associated with a deficiency of some as yet unisolated substance found normally in parts of the gastro-intestinal tract and embryologically associated organs. What causes this deficiency we do not know but it seems plausible to argue that it in turn must be secondary to some other infectious, developmental or metabolic disturbance. Dr. Dameshek has made it evident that, before we are to help our patients intelligently, they must be subjected to a more detailed study than we, as an average, are giving them today. I should like to ask him if he will go into more detail regarding the significance of jaundice as associated with various types of anemia in which it is found.

MEMBER: The case, which I shall report, came to my office in January, 1931, with symptoms of marked toxemia. The patient, who was unable to walk across the room, had fairly good color; her blood pressure was normal; examination of urine was negative. Toxemia test was negative. She had a little numbness of the fingers and toes, and difficulty in walking was quite apparent. A little later I did a blood examination and found she had red cells 2,700,000; white, 12,700. Liver and spleen were not enlarged. She had always been in good health, until she lost considerable weight in the last three months. Examination of the blood showed slight acidosis, practically no change in color or size,—the color count, 71-50%. She grew gradually worse and was soon unable to get out of bed or even to move from one side to the other. During that time her memory was impaired and she had difficulty in using her hands, or in fixing her attention. On account of the absence of hydrochloric acid she was put on liver extract, has been doing well ever since and has gained continuously. Toward the latter part of April, we extracted

some abscessed teeth. The last blood count was reds 4,540,000, whites 7,400. The improvement has been continuous and she now can walk around the room with the help of one crutch and go upstairs. She can ride in a car if helped in getting into it.

DR. DAMESHEK: In regard to the last case, it seems to be one of pernicious anemia with signs referable to the posterior columns of the spinal cord alone. Occasionally, one sees cases of this type in which the lesion is not a "combined system" disease but rather a single system involvement. Pernicious anemia without much anemia, but with marked involvement of the central nervous system, is not infrequent. This brings up the question of the dissociation of the bone marrow and the central nervous system lesions in the disease. Instead of liver extract, it is probably more advantageous in this type of case to use whole liver in large doses. Recently whole fresh ox-brain and liver extract preparations intramuscularly have been advocated. Dr. Robinson brought up the question of diagnosis of these "blood" cases in small communities. I think possibly that if one man in each community would take up blood work as more or less of a hobby and handle these cases, it would be a good thing not only for the community but for the man himself. In regard to jaundice in anemia, it is significant ordinarily of increased blood destruction. It is always important, in any instance of anemia, to determine the presence or absence of jaundice. Anemia without jaundice is not pernicious anemia; anemia with jaundice may be (and usually is) pernicious anemia. Regarding copper in the treatment of secondary anemia, I am not as yet prepared to state whether it is of actual benefit. I have used large doses of iron with good results in all cases of hypochromic anemia, whether these are secondary or "primary". Occasionally when the hemoglobin and red-blood cell count remain "fixed" at a certain level, the addition of copper in small amounts to the iron will result in marked improvement. Liver in the treatment of secondary anemia is, I feel, of minor importance. Whole liver, because of its iron and copper content, may be very slightly beneficial, but liver extract, even of the newer types which are alleged to be beneficial in secondary anemia, are, in my experience, worthless. Regarding "color index", since this depends upon an accurate hemoglobin estimation and an equally accurate erythrocyte count, it may at times be inexact and thus lead to false conclusions as to the type of anemia in a given case. A careful study of the bloodsmear especially with regard to the presence or absence of hypochromia and to the size of the red-blood cells is extremely helpful. Study of the white-blood cells and of the blood platelets in the same preparation gives us with the red cells a good idea as to the functional activity of the bone marrow. Quantitative estimations of the serum bilirubin (van den Bergh test) and study of the gastric contents are also important in the diagnosis of a "blood" case.

MISCELLANY

NEW MEMBERS

Dr. Edward Gideon Marcotte, Dover.
Dr. Bernard Joseph Manning, Jr., Dover.
Dr. Peter J. Doyle, Dover.
Dr. Arthur Winford White, Durham.

CHANGE OF ADDRESS

Dr. Clifford Howland, from Raymond to Brentwood, N. H.

Dr. Raymond G. Ingalls of Berlin has moved to Manchester, 839 Elm Street, and will limit his practice to diseases of the eye, ear, nose and throat.

RECENT ACCESSIONS TO THE MEDICAL PROFESSION IN NEW HAMPSHIRE

During 1931, twenty-seven physicians were licensed to practice medicine and surgery in New Hampshire, eighteen of whom are already located in the following towns and cities: Three in Hanover; two each in Concord, Wolfeboro and Dover; one each in Wilmot, Raymond, Bartlett, Henniker, Keene, Manchester, Ashland, Walpole and Center Ossipee. This is encouraging and indicates at least, in a measure, that the well-educated young physician is going back to the small towns.

The other men licensed are for the most part still training at various hospitals in other states considering this state as a possible location when their internship has been concluded.

ROCKINGHAM COUNTY MEDICAL SOCIETY

At a recent meeting of the Rockingham County Medical Society, the following officers were elected:

President: Joseph C. Tappan, Derry.

Vice President: Charles W. Hannaford, Portsmouth.

Secretary: John S. W. Knowlton, Exeter.

Treasurer: Wendell P. Clare, Portsmouth.

Delegate to State Society: John S. W. Knowlton, Exeter.

Committee on Medical Jurisprudence: Thomas W. Luce, Portsmouth.

Committee on Public Policy and Legislation: Samuel T. Ladd, A. W. Mitchell, Charles W. Hannaford.

Censors: E. A. Landman, T. W. Luce, L. R. Hazzard.

VERMONT STATE MEDICAL SOCIETY

THE SIGNIFICANCE OF THE BLOOD COUNT IN APPENDICITIS*

BY LYMAN ALLEN, M.D.†

STRANGELY enough the mortality of appendicitis is said to be rising in this country, in spite of all the study that has been put upon the disease, the number of cases seen annually, and the number of operations for the condition.

Perhaps we operate too often or upon too slight evidence of trouble with the appendix, but anyone who has seen the condition present inside the abdomen when an appendix has ruptured or has become gangrenous knows that such a patient is in grave danger of losing his life, and must realize that there was a time, either in this attack or in some previous one, when the appendix was merely congested and could have been removed with extremely little danger. So we are led to advise operation early, when, perhaps, the patient would have recovered from the present attack without operation, although he probably (though not certainly) would have had another attack later when the decision would have had to be made again.

In the series of cases which I am here reporting the mortality in these early or interval cases was zero, and so could not affect the mortality of appendicitis operations as a whole.

I believe that there are three reasons for the rising mortality of appendicitis in the United States:

1. Delay in operating.
2. Operations by unskilled men.
3. Mistaken diagnoses or those intentionally misstated, as when a young woman dies following a criminal abortion and the death is reported as appendicitis. But this is a digression and is not susceptible of proof.

We had but three deaths in this series of 200 cases, a mortality of one and one-half per cent. Two of the deaths were from general peritonitis and one from pneumonia on the sixth postoperative day, probably embolic in origin. This certainly is a good showing.

There were 18 cases which required drainage at the time of operation and all three deaths were from this number.

I am not one of those who believe that the appendix has some useful function and should therefore be let alone if not diseased. Of course the common practice is to remove the appendix as a routine in the course of other abdominal operations unless the extra time required and the slight extra shock be considered of sufficient moment to contraindicate it. This seems to me wise.

No doubt errors in diagnosis are made, both of omission and commission, and it behooves the surgeon to make sure that the patient with pain and tenderness in the right iliac fossa has not a pyelitis, cholecystitis, lead colic, pneumonia or even poliomyelitis or typhoid fever before he operates.

But today I am not considering especially the question of diagnosis, nor of whether to operate or not to operate, but the question of *when* to operate. We all see cases of right iliac pain which we diagnose as appendicitis, in which the question arises, "Shall this case be sent at once to the hospital for operation or will this attack quiet down, perhaps never to recur?" Perhaps for some reason this especial time may be most inconvenient for the patient to give up his work and take a month off—there is other illness in the family; or it is near the end of the student's school or college year and the delay of a few weeks would make the operation less of a calamity; or the business man is in the midst of some especially important undertaking; or the mother has a young baby whom it would be difficult to leave, etc., etc.

If we were sure in each individual case that immediate operation was essential, a mere matter of convenience would not count; the mother had better leave her baby for two weeks than forever, the loss of even a year to the student is much less important than the loss of his life, and few business transactions weigh more in the scale of living than life itself.

Again, when the patient has been sent to the hospital, perhaps from a considerable distance, and arrives in the evening, tired, frightened, perhaps weakened by a preceding sleepless night—when a good night's rest, even if the result of some sedative, would put him into much better condition to stand the operation—shall we operate at once or wait until the morning?

And there is the operating force and the surgeon himself to think of. After a hard day shall the operating force be routed out of bed to clean and prepare the operating room and then clean up afterward, a matter of perhaps three hours in the middle of the night, sandwiched in between days, each full of their own work? Will the surgeon operate as well at midnight as he would in the morning after his night's rest? Again neither the convenience of the hospital routine, the nurses, assistants nor

*Vice-president's address delivered at the Annual Meeting of the Vermont State Medical Society, October 8, 1931.

†Allen—Professor of Surgery, University of Vermont College of Medicine. For record and address of author see "This Week's Issue", page 1117.

surgeon should count if it is a question of increased safety of the patient. But is it? Is there any test or examination which will tell us with reasonable certainty whether we must operate tonight instead of in the morning?

It is with this in view that I am writing. For several years we at the Burlington hospitals have been guided by the blood count, taking the leucocyte and differential count together, and the opinion of the staff is fairly unanimous, I believe, that such count is of great value in determining the answer to the question "Shall we operate at once or may we safely wait a few hours?" The general appearance of the patient is no sure guide. Patients have many times walked into the hospital apparently in fair shape, when they had an appendix already gangrenous, and others looking much more ill have been found to have an appendix which did not demand immediate removal.

I had supposed that surgeons generally put the same reliance upon the leucocyte and differential count as we do, but rather recently I found that at one large hospital in New York City, and at another in Boston, the surgeons felt that such a count was of no special value.

In order to attempt to prove whether we were putting faith in an unreliable test I have reviewed the last 200 cases of appendicitis operated upon in the Mary Fletcher Hospital in the past year, using all the cases whose blood counts were complete and where there was no other condition found that might affect the count.

Dr. W. T. Rees did most of the arduous work of gathering the statistics and I have tabulated the results. The other members of the staff have given permission for the use of their cases. Several men made the actual blood counts and I know that this is a possible element of error, but the fact remains that these are the counts as made, upon which we decided either for or against immediate operation.

In general it is believed that the amount of the leucocytosis shows the resistance of the patient and that the percentage of "polys" indicates the virulence of the infection; therefore that the relation or ratio of these two factors should show the index of resistance of the patient to the given infection.

Taking 10,000 leucocytes and 70% of polys as normal, the index of resistance is shown as follows: (T-10)-(P-70) equals index of resistance.

E. G. If we have 16,000 leucocytes and 75% polys the Index of Resistance is (16-10)—(75-70) or 6-5 equals plus 1.

But if the polys were 80% and the leucocytes 16,000 the Index Resistance would be (16-10)—(80-70) or 6-10 equals minus 4.

Personally I do not think that this Index of Resistance is quite correct for appendicitis, for we have found that it is usually a minus figure. This is because, in that disease, a leucocytosis over 20,000 or 22,000 is rare (a rise of 10 or 12 above normal) while the polys may often be 85% to 90% (a rise of 15 to 20).

In this series of 200 cases, of those whose poly count was below 75%, four-fifths show a plus index of resistance and one-fifth a minus index of resistance. But of those whose poly count was between 75% and 80% the proportion was reversed and only one-fifth had a plus index of resistance and four-fifths a minus, and in the cases whose poly count was above 80% all had a minus index of resistance except two, which were zero.

The severity of these cases certainly did not vary proportionately to their index of resistance. One case with a minus 19¼ showed merely a Lane's kink and moderate inflammation of the appendix so far as gross appearances went, and the pathological report was "no suppuration, some infiltration, hemorrhage".

I shall not burden you with a prolonged discussion of the details of our statistics but almost without exception the findings at operation bore out the value of the leucocyte count and the percentage of polys together.

The actual leucocytosis alone is not sufficient—of the two the percentage of polys is the better guide. I arbitrarily divided the 200 cases into three groups according to the leucocytosis: 10,000 and below, of which there were 63 cases, 10,000 to 15,000, of which there were 80 cases, over 15,000 of which there were 57 cases. I also divided them into three groups according to the percentage of polys: 70% and below, of which there were 71 cases, 70% to 80% of which there were 65 cases, over 80%, of which there were 63 cases.

We found that of the 57 cases whose leucocyte count was over 15,000, 51 needed immediate operation and 6 might have been delayed with safety for a few hours at least. Of the cases having over 80% of polys, 64 in all, 58 required immediate operation and 6 might have waited—practically 10% in each group.

Therefore if the count is over 15,000 or over 80% of polys, operation should not be delayed. When the poly count was below 70% (and of course not over 15,000 leucocytes) all might have waited safely, and of the cases whose leucocytes count was not over 10,000 (and the polys not over 80%) all might have safely waited for some hours at least, except that those whose leucocyte count is very low (6,000 or less), should not be delayed for their resistance is impaired.

In the group whose poly count was between 70% and 80%—and the leucocytosis below 15,000, there were 50 cases, and almost all could have safely delayed operation—but as the leucocyte count approached 15,000 the condition was found more urgent.

Of the group of "drained" cases—18—fifteen had a leucocyte count of over 15,000 and 14 had a poly count of over 80%. All the 18 cases were

either over 15,000—or over 80%, or both,—except one, which had a count of 3,800 leucocytes and 69% polys. The tip of this appendix was gangrenous and it was one of the group of 8 cases under 6,000 leucocytes, all but one of which needed immediate operation.

In other words: (1) when the infection is so severe as to cause 80% or more of polys regardless of the total count, operation should not be delayed; (2) when the infection is such that it calls forth a reaction that gives over 15,000 leucocytes, even if the polys are low, operation should not be delayed. There were 14 of such cases and most of them needed immediate operation; (3) when the leucocyte count is very low (6,000 or less), regardless of the percentage of polys, it is safer to operate at once for something is wrong with the patient's resistance; (4) when the poly count is below 70% it is safe to wait if the total leucocyte count is under 15,000; (5) when the leucocyte count is below 10,000 and above 6,000 it is safe to delay, unless the polys are over 80%.

There are a number of cases (about 50 out of our 200) or one-fourth of all, which do not fall into any of these classes and must be called doubtful, and when in doubt it is safer to operate at once. But any method that will help us to decide the question of immediate operation or delay in three-fourths of all cases and with an accuracy of over 90% is surely worth using.

I feel that this small series of cases goes far toward justifying our faith in the leucocyte and differential count, and for the present at least, I shall continue to put confidence in it.

MISCELLANY

VERMONT DEPARTMENT OF PUBLIC HEALTH

OCTOBER, 1931

The prevalence of communicable diseases reported to this Department during October is shown in the following totals: Chicken pox 46, diphtheria 9, measles 78, mumps 25, typhoid fever 2, poliomyelitis 25, scarlet fever 21, smallpox 20, whooping cough 123, tuberculosis 21.

The Laboratory of Hygiene during October made a total of 1,412 examinations classified as follows:

Examinations	
For diphtheria bacilli	88
For Widal reaction of typhoid fever	33
For tubercle bacilli	215
For evidence of syphilis	434
For gonococci in pus	161
Of blood for contagious abortion in cattle	14
Of water, chemical and bacteriological	72
Of water, bacteriological	199
Of milk, market	71
Of milk, submitted for chemical only	0
Of milk, submitted for microscopical only	2
Of foods	1
For the courts, autopsies	6
For the courts, miscellaneous	44
Of animal heads for evidence of rabies	0
Miscellaneous	72

The Division of Communicable Diseases received reports of forty-one new cases of gonorrhea and forty-three new cases of syphilis. There were one hundred and ninety-six Wassermann outfits and one hundred and twenty gonorrheal slides distributed during the month.

The usual fall clinics were held at nine different points in the state, by the nurses of the Division of After-care for Poliomyelitis Patients. A total of one hundred and thirty-seven patients attended these clinics. Two hundred and forty-three patients were seen during October, one hundred and two at their homes and one hundred and thirty-seven at clinics and four at the office. One patient was admitted to the Children's Hospital in Boston, two were admitted to the Fenway Hospital in Boston, and three patients discharged from the Fenway Hospital. The vocational worker of this Division reports sales amounting to $244.86.

The State Advisory Nurse of the Maternity and Infancy Division visited nine towns, attending meetings and conventions held by various organizations such as Parent-Teacher Associations, Mothers' Clubs and social workers.

CHITTENDEN COUNTY

At the annual meeting held the last Thursday in September the following officers were elected:

President: Dr. P. K. French.
Vice President: Dr. A. L. Fogg.
Secretary and Treasurer: Dr. Sam Sparhawk.
Executive Committee: Dr. F. K. Jackson, Dr. W. T. Rees, Dr. A. B. Soule, Jr.

The retiring president's address by Dr. C. A. Ravey was entitled "The Treatment of Cutaneous Burns."

At the October meeting Dr. A. W. Rood of Springfield, Massachusetts, spoke on "Endoscopy."

ADDISON COUNTY MEDICAL SOCIETY

A meeting of the Addison County Medical Society was held at the Porter Memorial Hospital, Wednesday, October 28. Nine members were present. Two moving picture films were shown, on Simple Goitre and on Benign Hypertrophy of the Prostate. It was voted to continue showing similar films at later meetings. Dr. Dorey gave a report of the State Convention. ESTELLE FOOTE, M.D., *Secretary*.

OBITUARY

Dr. E. E. Dickerman, West Burke, Vt. A general practitioner of sterling qualities, he was born in Lyndon, Vt., May 11, 1859, and died in West Burke, Vt., November 7, 1931, after an illness of about five months, the result of a shock. He was actively engaged in the practice of medicine in West Burke from 1892 until May of the present year. He also practiced in Lunenburg, Vt., a short time before going to West Burke.

Dr. Dickerman received his preliminary education in Lyndon. He was a graduate of the University of Vermont Medical College and a Mason.

He is survived by Mrs. Dickerman and a daughter by a former marriage, Mrs. Mattie Leonard.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 17491

SIX MONTHS' FEVER

MEDICAL DEPARTMENT

An American brakeman thirty-one years old entered the hospital on May 27 complaining of fever every night for the past six months.

In November, six months before admission, the patient had fever, malaise, drowsiness and slight constipation. He was in bed for seven weeks under treatment for typhoid fever. He lost 65 pounds. At the end of seven weeks his abdomen began to swell. He vomited everything he ate and could not retain enemas. Operation was done. The surgeon reports that when he operated the patient had had phlebitis and partial intestinal obstruction. At the time of operation his condition was very poor. The surgeon found a retrocecal mass in the right iliac fossa extending over the brim of the pelvis. He did not find the appendix, but merely drained the tumor mass. A pathologic specimen showed merely inflammatory tissue, no tuberculosis or malignancy. The wound continued to drain for six weeks. Then it closed. After this he stopped vomiting and gained weight. He was discharged from the hospital in good condition on Easter Sunday. He continued however to have evening temperature of 101° to 102° which persisted from the onset of his illness until a few days before his entrance to the Massachusetts General Hospital. After two weeks at home he began to have lower abdominal pains which he thought were gas pains. He lost appetite, vomited once and was put back to bed. He was sent back to the hospital, where he gained, although the fever persisted. He had no cough at any time and no hemoptysis or bloody stools. His weight at admission was 108 pounds, a gain of 22 pounds in the past three months. His best weight was 145. He felt on admission that he was distinctly improving, and was troubled only by the evening temperature.

There was no history of familial disease.

His habits were good except that his rest was broken by the hours of his work. He had had the diseases of childhood, including scarlet fever. At seven years he had chorea and rheumatic fever, with recurrences at twelve and fifteen. Four months before admission he had migratory swelling of the joints treated with salicylates. For the past four months he had had blurring of vision. He urinated two or three times at night. He drank a great deal of water. The history was felt to be reliable except in the matter of dates and sequence of illnesses.

Physical examination showed a thin, pale, cadaverous looking young man lying quietly in bed in no acute distress. The lips were very pale. There were small petechiae on the left lower conjunctiva. There was marked pyorrhea. The throat was slightly red. There were two or three petechiae on the palate. At the angle of the jaw on each side was a gland the size of a hazelnut, not tender. The lungs were negative except for a few moist crepitant scattered râles at the left base posteriorly. The heart was markedly enlarged in all diameters. There was a precordial heave with bulging of the interspaces on systole. The rate was rapid and regular. At the apex there was a loud rumbling presystolic and an early systolic murmur shading into a midsystolic and late blowing systolic murmur. The first sound was muffled, diffuse and merging with the loud murmur. The second sound was very weak to absent. At the fourth space to the left of the sternum there was a similar picture except that the first sound was definite and the second sound could also be heard more clearly. At the third space to the left of the sternum there was a blowing presystolic murmur and a to and fro murmur, systolic and early diastolic. The first and second sounds were fairly clear. The aortic second sound was weak. The pulmonic second was accentuated. There was an atypical systolic thrill transmitted over the lower precordium. The pulses were normal. An electrocardiogram showed normal rhythm, rate 110, rather prominent P_1 and P_2. The abdomen was negative except that the liver edge was 2 fingerbreadths below the costal margin. There was a tender scar to the right of and slightly above the umbilicus. The extremities were atrophied. The right shin showed petechiae. The left ankle was slightly swollen, warm and tender.

The amount of urine was 37 to 90 ounces. The specific gravity was 1.012 to 1.022. The urine showed the slightest possible trace to a slight trace of albumin at four of five examinations. The sediment showed 2 to 12 leukocytes at three examinations, red cells twice, yeast once. Blood examination showed 9,300 to 27,800 white cells, 88 per cent polynuclears, hemoglobin 60 to 45 per cent, 3,160,000 to 3,630,000 red cells. Hinton and Widal tests were negative. The nonprotein nitrogen was 26 milligrams. The stools were negative to guaiac at both of two examinations.

The temperature was 98.9° to 103.7° with daily elevation until June 30, then a terminal drop to 97.2°. The pulse was 82 to 132, with one increase to 161 on June 26. The respirations were 16 to 40.

Fundus examination showed papilledema of

the right eye, 3 or 4 diopters of elevation. There was marked congestion and tortuosity of the retinal vessels. There were multiple extravasations and exudate. The left fundus showed 2 or 3 diopters of elevation with hemorrhagic areas throughout the fundus.

The patient slowly became weaker and more drowsy. He was treated with massive doses of vitamin A in the form of a concentrate in capsules. He continued to fail very slowly. June 23 he was very irrational and failed rapidly. He was given cod liver oil concentrate intramuscularly. He continued to fail. July 2 another electrocardiogram showed sino-auricular tachycardia, rate 130. The following day he was in deep coma. July 4 he died.

Clinical Discussion

BY RICHARD C. CABOT, M.D.,
TRACY B. MALLORY, M.D., AND
MAURICE FREMONT-SMITH, M.D.

NOTES ON THE HISTORY

Dr. Cabot: Of course we cannot be sure that that statement about fever every night for six months is accurate. Let us assume that it is. What are the diseases which could cause it? Tuberculosis is the commonest. The main question is, what is left after that? There are a number of cases of bacterial endocarditis which run for years. I have known certain cases which ran more than two years with fever every day. Then of course Hodgkin's disease can run for a long time. Abscess of the lung or bronchiectasis might, but ordinarily there are periods in which the pus is cleaned out and you have apyrexia for a time. Some of the bladder and kidney diseases with chronic suppuration in the kidney and bladder run fever for a long time. But ordinarily the striking thing is how the genito-urinary tract as a whole gets relatively immune so that little fever is caused. One can have more pus with less fever in the genito-urinary tract than anywhere I know. There are long cases of fever from necrotic tumors, especially in the liver, but I never knew one to run six months. No case of typhoid runs as long as that. We know typhoid can run with waves for three or four months' pyrexia with successive relapses. I do not know about undulant fever; I have no experience of that.

Dr. Mallory: It can run as long as this, Dr. Cabot,—up to three or four years in fact.

Dr. Cabot: I am glad to know that.

Dr. Fremont-Smith: Does the fever run constantly or are there apt to be periods without fever?

Dr. Mallory: An intermittent fever is certainly commoner.

Dr. Cabot: We will go on with those possibilities in the back of our minds. Of course tuberculosis and bacterial endocarditis are more probable than Hodgkin's disease, because the history of Hodgkin's disease generally gives us some other facts, such as pain or lump, in the visible foreground.

Swelling of the abdomen at the end of seven weeks is a very queer thing to have happen in typhoid. There we are expecting swelling of the abdomen early, not at the end of seven weeks. I do not remember any case of typhoid that showed that.

Phlebitis of course is a common complication or sequel of typhoid and might make the fever last.

Partial intestinal obstruction would not in itself contribute to the fever.

They "drained the tumor mass", so I take it there was something to drain. I take it that the surgeon did not consider it a neoplasm or he would not have expressed himself in that way. In that vicinity there might easily be a tuberculous mass which would have to be drained. That seems more probable than typhoid. But typhoid, since typhoid ulcers are near the ileocecal valve, might easily give us such an abscess.

Tuberculosis and sepsis are the things most in my mind so far, taking sepsis in the general sense; some perforation, very possibly from typhoid, having occurred in the region of the ileocecal valve, and sepsis, whether with internal phlebitis or other. You know of course that the three longest continued fevers that we see are typhoid, tuberculosis and sepsis, taking sepsis to include bacterial endocarditis and conditions such as this.

That history of chorea and rheumatic fever is important of course because it is the commonest basis or precursor of bacterial endocarditis.

The blurring of vision for the past four months is important as a possible evidence of nephritis or retinal emboli.

He urinated three or four times at night and drank a great deal of water—more things to suggest that he has glomerular nephritis, which often accompanies such a case.

NOTES ON THE PHYSICAL EXAMINATION

"Moist crepitant râles" is not good terminology. Crepitant is not ordinarily a word to be associated with other adjectives. Crepitant râles are not moist or dry or anything else.

In a patient as thin as I suppose this man was I do not think that a precordial heave, aside from the question of where it was, is important.

That electrocardiogram tends to make one think of mitral stenosis but is not in any way characteristic.

The abdomen was negative. I am surprised at that because of the tumor mass mentioned earlier. We have to take it to mean that the tumor mass was merely inflammatory and was effectually drained. Otherwise we might have wondered whether it was a necrotic neoplastic or tuberculous tumor. If the abdomen is nega-

tive, as it seems to be, I should think we could exclude both of those.

I do not suppose anyone takes that yeast in the urinary sediment seriously.

Of course the Widal at this time might have lasted on if it had been typhoid in the beginning.

The chart shows a terminal drop. Otherwise it is essentially a continued fever, with a pulse corresponding, not especially high or low in relation to the temperature.

The three things we think of in the fundus ordinarily are evidences of arteriosclerosis, evidences of nephritis and evidences of sepsis. I am rather surprised at the swelling. I do not altogether understand why there should be two or three diopters of elevation.

One tries any therapy that there is to try in such a case. I do not think anyone was very sanguine about the vitamin A therapy.

DIFFERENTIAL DIAGNOSIS

Much the most definite physical signs we have are those in the heart. We have not really at this time, in spite of the checkered history, anything to suggest disease in the abdomen, in the intestines or in the lungs.

We have a man who has had a marked rheumatic history, all we could possibly ask in the way of rheumatism, then what was called typhoid—I doubt very much whether it was. It was probably due to the same cause which brought about his death. After that "typhoid" he had abdominal swelling with the opening of a mass in the region of the ileocecal valve, with some phlebitis, we do not know just where. Then he apparently gets over the local signs of that inflammation, but continues to have fever, and comes here with cardiac signs but no cardiac symptoms. His symptoms were wholly those of sepsis, his physical signs those of cardiac disease, especially mitral. Some things also suggest an aortic lesion.

I want to go back to his urine again. He was probably having forced fluids. The gravity of the urine is normal. Four out of five times they found albumin, red cells only twice. I do not see how anyone can see there any distinctive evidence of nephritis. But the history and the condition of the eyes suggest nephritis. The nonprotein nitrogen does not. The anemia can be explained by fever and sepsis without supposing nephritis.

Bacterial endocarditis is the most probable diagnosis. It certainly would be my first guess. If he has local sepsis elsewhere in the body at present, as he may well have, I do not see that we have evidence of it.

Dr. Mallory ought to find a hypertrophied heart with an old mitral lesion, with presumably fresh vegetations, probably something on the aorta old or new or both. We have not enough evidence to say anything more definite about that. The petechiae mentioned are of course confirmatory evidence of bacterial endocarditis. I dare say that there was a blood culture and that we are not told about it.

Having committed myself, I will now ask for other diagnoses from the class.

A STUDENT: What further would you need to make a diagnosis of focal embolic nephritis?

DR. CABOT: We ought to have more blood in the urine. We are never very well satisfied even when we do have blood. That diagnosis is always more or less of a guess. He had blood only twice out of five times, and that was only microscopic.

A STUDENT: How would you explain the hemorrhagic patches in the disks except by focal embolic nephritis?

DR. CABOT: It seems to me they might be embolic. We do get embolism of the retina in bacterial endocarditis. I do not know enough to say this could not be embolism. The chief things that suggest nephritis are the etiology and some of the symptoms. There is nothing in the urine that is characteristic.

A STUDENT: What do you think that trouble in the right lower quadrant was?

DR. CABOT: I do not know what to think. The only thing I can imagine is a suppurating gland. I have seen suppurating glands not in just that region but in other parts of the abdomen in connection with this disease. I suppose it may have had some connection with phlebitis outside a gland. I have never known abdominal phlebitis of that type. Pylephlebitis produces such symptoms as this. It certainly cannot be the gall bladder. I do not know.

A STUDENT: Could that have been a typhoid complication? Could such inflammation in the right lower quadrant have existed without perforation?

DR. CABOT: I have never known it there without perforation, no. As I have known abscess like that from typhoid perforation, it always has been acute and practically always fatal. It must be rare if it is a chronic perforation of this kind.

DR. FREMONT-SMITH: Is a hazelnut-sized gland large enough to pay any attention to?

DR. CABOT: Yes, I think we ought to pay attention to it. But having paid attention I do not know what to think. If you feel a gland as big as a pea or as big as your finger tip you do not need any particular explanation. A hazelnut-sized gland should be explained. We have no evidence of local sepsis as far as I see to which it can be secondary, no evidence of neoplasm or syphilis. When we have considered those three things I do not see what else there is to think of. No one of them seems to fit.

Was there a blood culture?

MISS PAINTER: Two blood cultures showed streptococcus viridans.

DR. CABOT: I think there is nothing more to say.

CLINICAL DIAGNOSES (FROM HOSPITAL RECORD)

Rheumatic heart disease.
Subacute bacterial endocarditis.

DR. RICHARD C. CABOT'S DIAGNOSES

Rheumatic heart disease.
Subacute bacterial endocarditis, mitral, possibly also aortic.

ANATOMIC DIAGNOSES

1. *Primary disease.*

Rheumatic heart disease, chronic endocarditis of the mitral and aortic valves; mitral stenosis.
Subacute bacterial endocarditis.

2. *Secondary or terminal lesions.*

Embolic nephritis.
Infarcts in the spleen, the kidneys and the intestine.
Thrombus in a mesenteric vessel.
Beginning peritonitis.

3. *Historical landmarks.*

Islands of aberrant pancreas in the duodenum.

PATHOLOGIC DISCUSSION

DR. MALLORY: We found a definite subacute bacterial endocarditis on both the aortic and mitral valves, and as was expected, also chronic changes in both of those valves, including a well-marked mitral stenosis. On the whole bacterial endocarditis is much commoner on the mitral valves that do not show a marked degree of stenosis than on those that do. I think this is about as marked a stenosis as I have seen associated with bacterial endocarditis.

He did have a very extensive embolic nephritis. I cannot say whether the eye ground changes were due to that or not. However, as we did not have permission to examine the brain, it is possible that there may have been local lesions there.

There were infarcts in the spleen and kidneys, as there usually are in these cases, also the less usual complication of infarcts of the intestine. The terminal portion of the ileum and the major portion of the cecum were gangrenous and a thrombus was found in one of the mesenteric vessels. I can only guess as to what he had six months ago, but I suspect it was the same thing, a mesenteric embolus which did not completely occlude the vessel and from which he recovered. Mesenteric thrombosis would be a remarkable thing to recover from. But I have known of cases of gangrene of the intestinal tract which have recovered spontaneously.

DR. CABOT: What do you suppose was the tumor mass that they drained?

DR. MALLORY: I think there is very little doubt that he had an abscess above the cecum. Whether that first area of necrosis in the intestine was in the appendix or the cecum or the terminal ileum I cannot say. There was evidence of scarring in the appendix, also evidence of fresh necrosis.

The only other finding of interest was a congenital anomaly, islands of aberrant pancreas. It is perfectly possible that those may be large enough to cause pyloric obstruction. In this instance they apparently produced no symptoms.

DR. CABOT: Can you tell typhoid as late as this, six months after the disease?

DR. MALLORY: I am not perfectly sure that I can. On the other hand typhoid would not account for thrombosis of the mesenteric artery. It might account for a venous thrombus, but not for plugging of the artery. It seems to me that if he had had typhoid six months ago the Widal would be still positive. The Widal usually remains positive for a year following vaccination or following an attack of typhoid.

A STUDENT: Did you investigate the swollen glands?

DR. MALLORY: No, we did not. Those in the mesentery were secondary to beginning peritonitis.

DR. FREMONT-SMITH: With nephritis sufficient to give marked choking of the disks shouldn't you expect the non-protein nitrogen to go up?

DR. MALLORY: Yes, I should. Of course this embolic nephritis that we get in bacterial endocarditis rarely gives renal insufficiency. The important thing in producing symptoms in nephritis is to have a lesion involving every glomerulus. If you have a lesion which picks out some glomeruli and leaves others the kidneys will function; and you know you can remove one kidney and the person will get along perfectly well. Embolic lesions would not ordinarily produce renal insufficiency.

DR. FREMONT-SMITH: Then why the choked disks?

DR. MALLORY: I am puzzled about that. I wonder if he did not have a cerebral lesion which we did not have a chance to find.

CASE 17492

AN UNUSUAL CASE OF GRADUAL ONSET OF COMA

MEDICAL DEPARTMENT

An American chauffeur of thirty entered on April 28 in coma. The history was given by his wife.

On April 25 he "caught cold". The next day he felt ill. On April 27 he had blurred vision. After working only a few minutes that morning he was brought home and went to bed. He complained of headache and of tingling, first

in the left foot and arm, later in the whole left side, then in the right arm. He complained of severe pain in the back, then became comatose, frothing thick mucus from the mouth at first. He had several severe chills during the first part of the night and was stuporous all night. His wife thought he was not paralyzed. He moved his left leg. In the morning his condition was much worse.

His father and mother both died of tuberculosis. There is no history of familial disease.

The past history is negative except that for the past six months he had slept all the time when not working or eating, and had been unusually irritable and rude.

Clinical examination showed a desperately sick man in extreme respiratory distress and deep coma. The skin was pale, hot and moist. The mucous membranes were moderately cyanotic. There were blisters on both ankles. There was very marked pyorrhea and dental caries. The respiration was very rapid. The chest was filled with bubbling râles, with slight impairment to percussion and distant breath sounds at the left base. The heart and abdomen were normal. The muscles of the right hand showed atrophy. All the reflexes were hyperactive. There was positive Babinski on the left and slight poorly sustained bilateral ankle clonus. The pupils and fundi were normal.

Urine examination showed a specific gravity of 1.035 and a large trace of albumin at one of two examinations. Blood examination showed 31,800 to 17,200 white cells, 90 per cent polynuclears, 4 per cent eosinophils, hemoglobin 80 per cent, reds 5,000,000, smear normal. The carbon dioxide combining power was 51 per cent. A Hinton test was strongly positive.

The temperature was 104.5° to 109°, the pulse 115 to 122. The respirations were 37 to 35.

X-ray examination showed the diaphragm normal in outline. The lung fields were clear. There was some prominence of the lung markings.

The visiting physician noted, "The breathing suggests laryngeal or tracheal obstruction. He will develop some stieky sputum by cough and then breathe more easily for a bit. The lungs are resonant throughout, without bronchial breathing anywhere. The tracheal noises are transmitted everywhere. . . . . Lumbar puncture was discussed and decided against as in a moribund patient an unjustifiable procedure."

A throat consultant found no evidence of membrane or follicular spots in the nose, throat, pharynx or larynx. There was a profuse amount of mucopus brought up from the bronchi. The upper tracheal rings showed reddening only. There was no evidence of tumor or vocal cord paralysis.

A surprising factor in the case was the rapid and extraordinarily deep respiration, suggesting acidosis, which was not present.

The patient went rapidly downhill from admission. Oxygen tent, intravenous glucose and supportive treatment were without result. The temperature rose steadily to 109°. The patient died of respiratory failure on the afternoon of admission.

Clinical Discussion

BY MAURICE FREMONT-SMITH, M.D., TRACY B. MALLORY, M.D., AND ARVID LINDAU, M.D.

NOTES ON THE HISTORY

Dr. Fremont-Smith: Pneumonia sometimes has an onset of extreme rapidity, so that the patient is well in the morning and by night is in coma. I suppose it is quite possible that the coma is due to a sudden increase in intracranial pressure, i.e., meningismus. I do not know whether it is always due to that or not. It may also be due to the toxin of pneumonia.

The blurred vision that came on the day before he was taken here is of course a very important symptom. We associate it with nephritis or with increased intracranial pressure.

Of course we may be dealing with a cerebral accident; the sudden onset and the blurred vision make one think of that possibility. Then we have tingling and numbness, first in the left foot and arm, later on the whole left side, which make one think of a right cerebral lesion behind the motor area in the sensory area. We find it later in the right arm. That gives us a good deal about localization. It requires a hemorrhage that is very large to involve both those areas. Of course we are dealing with the brain. We know we are not dealing with the cord alone because he has cerebral symptoms. A lesion on one side of the brain is compatible with life. Where we have disturbances of both sides it implies that the lesion extends over the brain from one side to the other. Usually under those conditions the hemorrhage is so great that it causes death. Consequently we hesitate to say cerebral hemorrhage here. If this is a vascular accident it is more likely to be thrombosis, although there again we have the same difficulty. The thrombosis must be a very large one. We will ask Dr. Mallory whether thrombosis could involve the sensory areas on both sides.

Dr. Mallory: It hardly seems possible.

Dr. Fremont-Smith: This man is thirty years old. He is very young for either hemorrhage or thrombosis. So I am so far quite in the dark.

He had severe pain in his back, besides the other symptoms. Perhaps the best way to put that all together is to conceive of a meningitis of sudden onset with increased intracranial pressure, with blurring of vision, with involvement of the cortex of the sensory area. Yet of course with meningitis headache is usually far more prominent than backache. In mild meningitis

such as we see in poliomyelitis sometimes the patient has more back pain than head pain.

The frothing of mucus might imply that the ninth and tenth nerves were involved or it might be due to difficulty in swallowing mucus resulting from the fact that he was so comatose that normal stimulus to deglutition was not effective.

This whole picture of the present illness could come from another type of vascular accident, that is subarachnoid hemorrhage. Subarachnoid hemorrhage comes on in early youth, even at the age of fifteen. The onset is very sudden usually, more sudden than in this case, although I suppose one could conceive of a small leak. Almost always subarachnoid hemorrhage begins with severe headache and stiff neck; later if the hemorrhage is large enough there are signs of increased pressure resulting in coma, sometimes death—and sometimes recovery.

There is one thing I have learned through personal experience and that is that one has to be very careful in draining the spinal canal in subarachnoid hemorrhage. One does a lumbar puncture and finds bloody fluid with increased pressure. One should lower the pressure, but not too much. A very good rule is to bring it down one-half, and six hours later bring it down to one-half what it was the second time.

His father and mother both died of tuberculosis. Could this be tuberculosis? No tuberculous meningitis begins as suddenly as this. The characteristic onset is very slow. In a child there is usually lack of appetite, some headache and change in character. The child is not very sick at first. Then gradually over a period of days or a week or two the picture becomes more definite. This is not the picture of tuberculous meningitis, and I cannot think of any other form of tuberculosis which this could be. Could he be suffering from one of the other causes of coma? We have spoken of nephritis. That still has to be kept under consideration. Could it be diabetic coma? I do not know of any facts on which to base the diagnosis. In diabetic coma pain, headache and blurring of vision are not characteristic. I should say they do not occur.

For the past six months the patient had slept all the time when not eating and had been unusually irritable and rude. That gives us a hint. Evidently this trouble did not start three days before admission; it started six months ago. We can very easily fit that in with the present picture, supposing he had a tumor, and supposing that was growing very slowly and giving very little evidence of its presence. We all know that a tumor can grow to large dimensions in a silent part of the brain causing no symptoms. The first symptom may be a sudden attack of convulsions. When we see a patient with sudden onset of convulsions one of the things to think of is brain tumor. Or there may be a period of rapidly increasing coma. What happens under those circumstances? Either there is hemorrhage into the tumor or the tumor presses on some area which prevents the normal flow of spinal fluid, resulting in sudden increase in intracranial pressure. This is not an acute meningitis. It may very well be a picture of tumor with sudden hemorrhage or blocking.

NOTES ON THE PHYSICAL EXAMINATION

I should like to know more about his respirations, whether they were Cheyne-Stokes in character or whether they were very deep and full such as one might find in acidosis.

The skin was hot and moist. The skin in diabetic coma is dry. The skin of an insulin shock patient is wet.

Those blisters on both ankles mean nothing to me. Has anybody any suggestions?

A STUDENT: Perhaps he had had mustard plasters.

DR. FREMONT-SMITH: Marked pyorrhea and dental caries mean nothing in connection with this, and very little anyway, because one finds so many people who have them.

One would not expect very rapid respiration with increased intracranial pressure. That makes us think again of pneumonia. When we get pneumonia with extremely rapid respiration and air hunger we can give a poor prognosis. I have gone out to get a nurse for a patient breathing that way and have come back to find him dead.

The bubbling râles in the chest, percussion impairment and distant breath sounds at the left base may mean something or they may mean very little.

"The muscles of the right hand showed atrophy." I wonder if he was left-handed. I do not see how we can fit that in with any condition we are considering. Atrophy, if it is due to a central nervous system lesion, is due to a lesion of the peripheral neurons, to a lesion in the anterior horn cell or peripheral nerve. If this is a lesion of the head there is no possible place in the brain cortex or in the internal capsule or anywhere above the anterior horn cells that can give atrophy. Syringomyelia hits the anterior horn cell by pressure from the inside of the cord, so that we get atrophy because the anterior horn cells are thrown out. We get the same thing in poliomyelitis and in a myotrophic lateral sclerosis. We are far above the anterior horn cells if we are dealing with a brain lesion. That atrophy is also unexplained.

Of course we should not expect hyperactive reflexes with atrophy. If hyperactive reflexes are due to a central nervous system lesion and not to strychnine poisoning or other toxin or simply to the nervous make-up, they must be due to something above the anterior horn cells. We must postulate a lesion in the cortex, intimal capsule or pyramidal tract. So those two things, atrophy and increased reflexes, do not go together.

With the slight poorly sustained bilateral ankle clonus we have another reason for feeling that there is an injury to the pyramidal tract. Where is it? It cannot be in the cord alone because then we should have no cerebral symptoms. If it were in the cord one might easily have bilateral symptoms. A little compression in the cord can give bilateral symptoms, but in the head it is more difficult to get them. If we assume it is in the head we have evidence that it is chiefly on the right side because of the tingling of the left foot and arm. Why the fundi were negative it is hard to say if you assume increased pressure except that where there is increased intracranial pressure it takes time, sometimes a number of hours and sometimes a few days, before the disks become choked.

The specific gravity of the urine was 1.035. He probably had not been drinking much water during the last twenty-four hours. At one examination there was a large trace of albumin; at the other examination there was no albumin. I do not think we have to explain that on the basis of a kidney lesion. We get albumin often without any kidney lesion.

I do not know whether or not to place any reliance on the strongly positive Hinton test. I should like to. If we can it brings up one other possibility, that is an acute luetic meningitis. Of course it would strengthen our feeling that he may have had a subarachnoid hemorrhage, although most subarachnoid hemorrhages are not luetic, not caused by luetic aneurysms. Has he luetic meningitis? The acute part of the disease is very acute for this disease. Of course the lumbar puncture is going to help us and I think it is fair to wait for that. Has any one of you looked up the clinical course of luetic meningitis?

A STUDENT: I looked it up in Osler. He emphasizes the resemblance of it to brain tumor and its chronic course in the beginning. He does not say anything about the white blood cell count.

DR. FREMONT-SMITH: I do not think it would be high.

DR. LINDAU: Luetic meningitis may set in suddenly, though that does not occur very often. It characteristically involves the eye muscles when it sets in suddenly.

DR. FREMONT-SMITH: Do you think this story would be consistent with luetic meningitis?

DR. LINDAU: It is very hard to say.

DR. FREMONT-SMITH: The respiratory rate is fast, but not very fast. We do find respiratory rates of 65.

What made the throat consultant think of laryngeal or tracheal obstruction?

A STUDENT: The whistling sound of the breathing.

DR. FREMONT-SMITH: The same sort of sound you would make if you squeezed your larynx. It is a very definite sound and I think usually means laryngeal or tracheal obstruction. Evidently it made them think it might be a case of diphtheria or a diphtheritic membrane.

The temperature again rather suggests some intracranial condition I should say. Usually patients with pneumonia do not have so high a temperature as that unless the heat regulating mechanism is entirely knocked out, and I think it is more apt to be knocked out from an intracranial lesion than from toxin such as pneumonia.

I am absolutely in the dark as far as giving a definite diagnosis is concerned. Have any of you worked out a definite idea?

STUDENTS: Syphilitic meningitis. Streptococcus septicemia. Cerebral abscess with terminal meningitis. Tuberculoma. Bronchopneumonia with cerebral symptoms. Cerebrospinal fever. Meningococcus meningitis.

DR. FREMONT-SMITH: I am going to base my diagnosis simply on the past history. We do not know whether the history is correct or not, but if it is true that he has been changing in character and has slept all the time when not working, that must mean something. I am going to say brain tumor.

CLINICAL DIAGNOSES (FROM HOSPITAL RECORD)

Pyrexia of unknown origin.
Brain abscess.

DR. MAURICE FREMONT-SMITH'S DIAGNOSIS

Brain tumor.

ANATOMIC DIAGNOSES

Luetic meningitis and encephalitis.
Acute influenzal pneumonia.

PATHOLOGIC DISCUSSION

DR. MALLORY: I am not quite sure I know the whole story of this case.

We found two definite and I think entirely independent lesions. One of them was a chronic type of infection of the meninges and brain substance with a good deal of perivascular infiltration of plasma cells pretty well scattered throughout the brain substance. Lesions of the same type were found in the meninges as well, though here we found some scattered polynuclears also. There was, however, no true acute meningitis.

The other striking feature of the case was the lungs. All five lobes of both lungs were greatly enlarged, extremely edematous and hemorrhagic. No lobe was entirely consolidated and yet no lobe was of normal consistency. A great many alveoli appeared in gross to contain a hemorrhagic, very thin fluid exudate. On gross examination I did not feel sure whether it was pneumonia or not. When it came to microscopic examination we found that throughout the lung there was a hemorrhagic and serous

exudate in the alveoli; almost no leukocytes, no fibrin. The alveolar walls showed a peculiar hyalin necrosis which is very characteristic of and I think probably pathognomonic of the so-called influenzal pneumonia. This man died last April. During a period of four weeks then we had five cases with this same type of pneumonia. There were no cases in the preceding twelve months and there have been none since. Clinically there was typical influenza in the city at that time.

Cultures from the lung showed non-hemolytic streptococcus and no influenza bacilli. I had expected that we should at least find a hemolytic streptococcus.

Blood cultures and cultures from the meninges were negative. Dr. Kubik felt that the brain lesions were probably those of a chronic, slowly progressive luetic meningitis. They certainly antedated by weeks or months the acute pulmonary lesions.

I think we have to make two diagnoses, luetic meningitis and encephalitis with acute influenzal pneumonia as the terminal event.

Dr. Fremont-Smith: It is interesting that the x-rays showed nothing at all in the lungs.

Dr. Mallory: I should expect that from the appearance of the lungs at autopsy. Every lobe was involved and yet no area was really consolidated. There was none of the thick fibrin and leukocytic infiltration one gets in pneumococcus pneumonia.

A Student: Was there any lesion in the brain that would account for the high temperature?

Dr. Mallory: No single definite lesion certainly. I should be a little inclined to connect the temperature with his influenzal pneumonia rather than with the meningitis, which was apparently a chronic affair and had not really troubled him much until this last illness. One very atypical thing about it was his white cell count, if it really was influenzal pneumonia. A white cell count of 30,000 is very unusual.

Dr. Fremont-Smith: What would lumbar puncture have shown if it had been done?

Dr. Mallory: I think it would have shown a few lymphocytes. There was very little exudate in the subarachnoid space, none in gross, only on microscopic examination.

Dr. Lindau: I wonder if there were any hemorrhagic lesions. That is most usual in influenzal encephalitis. We have hemorrhagic lesions giving the well-known and easily recognized picture of a purpura cerebri at postmortem. In certain epidemics as many as 30 per cent of the cases have been complicated with encephalitis (Schmorl). That is a much more common complication than meningitis. About six months ago I had a section on one case in which the patient died so suddenly that we suspected he had been poisoned. I found hemorrhagic encephalitis and influenza too. There were only slight changes in the lungs. There is no correspondence between the changes in the lungs and those in the brain, because often I think the infection is so heavy and virulent that it does not stop in the lungs but we immediately get brain changes and the patient dies in a few days.

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THE COFFEY-HUMBER TREATMENT IN LIGHT OF AUTOPSY FINDINGS

AN interesting aftermath of the cases treated with the Coffey-Humber suprarenal extract is presented by a report of Ball[1] in the *American Journal of Cancer*. His conclusions are based on 89 cases which received the Coffey-Humber treatment. They are compared with 27 other cases which constitute the control series. The total, 116 cases, are divided into this control series in which no suprarenal cortex was administered; a second control or inadequately treated series in which not more than 10.5 c.c. of the adrenal cortex was administered, 47 in number; and a series of 42 cases, all of which were given more than 10.5 c.c. of the extract (usually more than 15 treatments).

The cases are fairly widely distributed, ranging from carcinoma of the stomach, breast and cervix, as the most frequent, to primary cancer of the liver and melanoma, the least frequent. Inasmuch as Coffey and Humber claimed in their patent application that the chief changes produced in malignant tumors as a result of their treatment are necrosis and sloughing, Ball devoted particular attention to this point. The degree of necrosis was judged primarily on gross observation and controlled with microscopic examination.

The amount of necrosis in all three series roughly paralleled that reported by Coffey and Humber in their first group and was materially less than that reported by them in their second, or more adequately treated group. It is of interest that the degree of necrosis reported by Coffey and Humber in their first group does not exceed that in untreated, or in what might be termed inadequately treated cases. Moreover, even should sloughing be accelerated, it may be a distinct disadvantage to the patient through massive hemorrhage and extensive pyogenic infection.

Perhaps the strongest indictment against the suprarenal extract treatment is the report by Harris[2] based on observations of 415 treated cases, which states "Malignant tumors were observed to increase in size, and new extensions and metastases to occur in many patients during the time that they were receiving the extract injections."

These reports leave but little excuse for continuing this extensively exploited treatment for malignant disease.

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THE SMOKE EVIL

ALTHOUGH doctors have tried to arouse general interest in the smoke nuisance because of its economic burden and health hazard, much remains to be done in eliminating this annoying and dangerous complication of modern civilization.

We must have artificial heat and power which are produced by combustion. Unfortunately no economic method has been found for the complete oxidization of carbon, and the unconsumed element makes a city untidy, obscures the sun's rays and when inhaled is an irritant to the mucous membranes.

In all large cities smoke abatement commissions are studying these problems, but the appeal of physicians and the cry for relief from the laity cannot lead to effective reform until engineers and manufacturers find ways to burn coal and oil more completely than is possible in the present state of our knowledge and consistent with economy.

The conversion of all the carbon of coal and oil into heat and power units is theoretically possible, but is not attainable at the present time. Commissions have made regulations, but they seem to be ignored or it may be that stokers have not the time or intelligence to feed heaters in a more effective way.

To those who have paid little attention to this

subject we suggest climbing to a commanding height at the time when stokers pay their last visit of the day to furnaces in the winter.

Practically from every building volumes of smoke pour out for a time until the more volatile constituents of the fuel have been thrown off.

This is also to be noted if one rises at a time when the fires are tended in the morning and at intervals throughout the day.

It is the opinion of scientists that an atmosphere polluted in this way obstructs the passage of valuable sun rays and everyone understands that inspired smoke is not wholesome.

Such opinions were recently voiced in a meeting of the New York Academy of Medicine, but the doctors seem to be helpless in bringing about reform until engineers will find ways to insure better combustion and smoke nuisance commissions require more loyal observance of regulations. It is an old subject but still of vital importance. The medical profession should use its influence to bring about better conditions.

A PETITION FOR AN EXTENSION OF THE CHARTER OF THE UNIVERSITY OF MASSACHUSETTS, INC.

A GROUP of citizens of Massachusetts has appealed to the legislature of this state for a change in the charter of the University of Massachusetts, Inc., which will authorize the granting of degrees of Bachelor of Science to its graduates as appears in full in the copy of the petition below:

TO THE HONORABLE SENATE AND HOUSE OF REPRESENTATIVES OF THE COMMONWEALTH OF MASSACHUSETTS IN GENERAL COURT ASSEMBLED

The undersigned, citizens of the Commonwealth of Massachusetts, respectfully represent that the University of Massachusetts, Inc., is an institution of learning duly organized under the General Laws of the Commonwealth in 1917 for educational purposes; that since 1917 this corporation has conducted college courses for the instruction of students possessing a high school education or its equivalent; that these courses have been designed to conform with the requirements for admission to medical schools and have been given in affiliation with the Middlesex College of Medicine and Surgery, Inc., that there are at present enrolled in this college over one hundred students; that this corporation through its affiliation with the Middlesex College of Medicine and Surgery, Inc., has the use of extensive school buildings for classrooms and laboratories;

WHEREFORE, your petitioners pray that this corporation, in following the present trend of advanced premedical requirements, may be granted the authority to confer the degree of Bachelor of Science upon its graduates who have completed a full four-year course of collegiate instruction, or three years of collegiate instruction followed by the completion of a four-year course of medical instruction in its affiliated institution, the Middlesex College of Medicine and Surgery, Inc.

C. RUGGLES SMITH, 473 Beacon Street, Boston.
JOHN M. RUSSELL, 11 Beacon Street, Boston.
GEORGE P. TILTON, 25 Audubon Road, Boston.
PATRICK J. DUANE, Mayor of Waltham.
FRANCIS B. SEARS, 21 Crescent Street, Weston.
H. F. WHITTEMORE, 24 Federal Street, Boston.

It has been a matter of surprise to many that a charter using in its title the words "University of Massachusetts" should have been granted, inasmuch as the use of this title seems to convey the impression that this is a state university, whereas the Commonwealth of Massachusetts as such is not represented on the managing boards of this organization.

This University of Massachusetts, Inc., has as one of its departments the Middlesex College of Medicine and Surgery which several years ago took over the charter of a medical school formerly located in Worcester, Mass. The Worcester Institution had not been functioning as a medical school for several years prior to the transfer of the charter to the Middlesex College of Medicine and Surgery. With this change a comparatively new medical school was organized and carried on its work for several years in a building in Cambridge, Mass. A new building has been erected in Waltham, Mass. The Middlesex College of Medicine and Surgery was never given an endorsement by the Council on Medical Education and Hospitals of the American Medical Association and has not permitted an examination of its plant or curriculum by this Council, and its graduates have been denied admission to examinations of a large majority of the medical registration boards of this country.

It may be that the University of Massachusetts is planning to qualify the students in its academic department for matriculation in the Middlesex College of Medicine and Surgery and thus meet the somewhat indefinite requirements of the present Massachusetts law for a premedical education.

While we believe in democracy in medicine and every opportunity for institutions to aspire to useful positions in the field of education, we believe that no school can safely keep aloof from organizations which may be helpful and stimulating.

Until the University of Massachusetts, Inc., and the Middlesex College of Medicine and Surgery adopt a different attitude, they will continue to be outlaws in most of the states.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

COCHRANE, ROBERT C. S.B., M.D. Harvard University Medical School 1911. F.A.C.S. Surgeon-in-Chief, Boston City Hospital. Assistant Professor of Surgery, Harvard Medical School. Consulting Surgeon to Boston Lying-In Hospital, Leonard Morse Hospital, Natick, and Framingham Hospital. Address: 319 Longwood Avenue, Boston. Associated with him is:

NOWAK, STANLEY J. G. A.B., M.D. Harvard University Medical School 1926. Associate Sur-

geon to Fifth Surgical Service, Boston City Hospital. Instructor in Surgery, Harvard Medical School. Address: Boston City Hospital, Boston. Their subject is: "Dermoid Cysts and Teratomata of the Mediastinum." Page 1077.

CLUTE, HOWARD M. B.S., M.D. Dartmouth Medical School 1914. F.A.C.S. Surgeon, Lahey Clinic and Assistant Surgeon, New England Baptist Hospital. His subject is: "Clinical Aspects of Thyroid Malignancy." Page 1083. Address: 605 Commonwealth Avenue, Boston.

KEFFER, CHESTER S. B.S., M.S., M.D. Johns Hopkins University 1922. Assistant Professor of Medicine, Harvard University. Associate Physician, Thorndike Memorial Laboratory, Boston City Hospital. His subject is: "Some Clinical Aspects of Deficiency Diseases." Page 1086. Address: Thorndike Memorial Laboratory, Boston City Hospital, Boston.

DAMESHEK, WILLIAM. M.D. Physician to the Blood Clinic of the Beth Israel Hospital and the Boston Dispensary. Harvard University Medical School 1923. Instructor in Laboratory Medicine, Tufts College Medical School. Assistant in Medicine, Beth Israel Hospital. His subject is: "Some Types of 'Primary' Anemia and Their Treatment." Page 1093. Address: 484 Commonwealth Avenue, Boston.

ALLEN, LYMAN. B.A., M.Sc., M.D. University of Vermont College of Medicine 1896. F.A.C.S. Professor of Surgery, University of Vermont College of Medicine. Surgeon, Mary Fletcher and Bishop De Goesbriand Hospitals. Consulting Surgeon, Fanny Allen Hospital. His subject is: "The Significance of the Blood Count in Appendicitis." Page 1105. Address: Burlington, Vermont.

THE BOSTON MEDICAL LIBRARY

MICHAEL SERVETUS
1509-(11)-1553

THERE is scarcely a more tragic character in medical history than that of Michael Servetus. If, before some impartial tribunal, those who, in this life, have been instrumental in checking the advancement of human thought through their shortsightedness and bigotry, shall receive a hearing, the ones who placed a stumbling-block in the pathway of Servetus will have much for which they must answer. He was a Spaniard by birth, whether of Aragon or Navarre is not quite certain. Neither is it fully determined whether he was born in 1509 or 1511. The data upon which both of these points rest were derived from Servetus himself and he is dead. At his trial for heresy before the Inquisition he gave Tudela, in Navarre, as his birthplace and his age as 42. Four months later, at his Geneva trial, he claimed that Villanova, in Aragon, was his native place and his age 44. There were reasons why he should have given this misinformation for in both cases he was on trial for his life. Not much is known of his ancestry except that he came from a family of Jurists, was of gentle blood and a Christian, i.e., he was not of Moorish or Jewish descent. His parents intended that he should prepare himself for the service of the Church. In fact piety coupled with intellectual precocity characterized his youth. He apparently received his early instruction in a cloister under the direction of a more than usually learned monk. He left the environment of the convent before vows were exacted which would have committed him to the priesthood. At about his twelfth year he entered the University of Saragossa where he came under the influence of one of the most liberal-minded and accomplished men of the age, viz., Peter Myrtyr Angleria. He remained under this influence four or five years perfecting his knowledge of the classics, the ethics of Aristotle and scholastic philosophy as well as mathematics, astronomy and geography. Having grounded himself along these general lines and definitely abandoned the thought of the Church, he turned to the law, the profession of his ancestors, and was sent by his father to Toulouse. While here he became interested in the study of the Scriptures and through them and such other literature and instruction as he was able to have the benefit of, he came to seek for demonstrations of God's revelation of himself in nature. The teachings of Erasmus and Luther filtered through the obstacles put up by the priests to prevent contamination of the mind of youth with heretical ideas and Servetus was quick to grasp them. His knowledge of Latin, Greek and Hebrew, together with his familiarity with Ptolemy's Geography and with History served to open his mind to liberalizing influences and forced him to run counter in his thought and belief to much of the teaching of his generation. His stay at Toulouse was interrupted by the invitation of a Franciscan Friar, Juan Quintana, who was confessor to the Emperor, Charles V, to be present at the coronation exercises at Bologna and later to attend the Diet of Augsburg. This was in the summer of 1530. Here he was brought in touch with Melancthon and other leaders of the Reformation and must have had opportunity to observe much that compelled him to repudiate the doctrines of the established religions. At any rate not long after, in this same year, he is heard of at Basle, severely arraigning the theological concepts of the time. Perhaps because of this he received his dismissal from the retinue of the Emperor, after not over 18 months of service.

He spent two years in Switzerland engaged in polemic discussions with Zwingli and other of the Reformers, wrote his "De Trinitatis Erro-

ribus" and had it published. In consequence of the ferment into which this work precipitated the Swiss reformers, Servetus thought it wise to quit Basle for Paris where he arrived in 1532 and entered upon the study of mathematics and Physics at one of the colleges and later is said to have taken the degrees of M.A. and M.D. from the University of Paris though there is no record of this. Here he assumed the name of Villaneuve. He wrote and edited numerous works under this name at Lyons while he practiced medicine for 14 years at Vienne, a neighboring town. It was on the occasion of his return to Paris that he made his first contacts with John Calvin and sought to engage him in public debate upon the theological questions that interested them both. This never came about. While pursuing his medical studies he was brought in touch with two of the great reformers in medical teaching, viz., Vesalius, who was a fellow student and Guinther of Andernach and Sylvius the renowned Professors of Anatomy. Servetus and Vesalius were prosectors for the Professor. It was while working here that Servetus inferred the existence of the pulmonary circulation from the structure of the heart and lungs, thus foreshadowing Harvey's great physiologic discovery. It is of interest to recall that Vesalius met his death as the sequel of shipwreck while returning from the Holy Land where he had gone in expiation of a charge of murder growing out of a postmortem he performed upon a patient whose friends claimed he was not dead when Vesalius made the section. The publication that was the occasion of Servetus' tragic ending was the one in which he first published his ideas upon the pulmonary circulation, though it was not that doctrine to which exception was taken by Calvin and his other accusers. In order, probably, to secure an income while waiting for practice as well as to satisfy his desire to teach, he offered a course of lectures upon the Geography of Ptolemy and the science of Astrology which were highly successful from a pecuniary point of view and also because of the friends he made through them. He entered the field of medical publication at this time by publishing a treatise on "Syrups and their use in Medicine." His other excursion into the medical lecture field was not so successful for it led to his being prohibited from giving any other lectures on the subject of divination or astrology on pain of being deprived of his doctor's degree. After this discipline he withdrew again from Paris to another suburb of Lyons where he resumed the practice of medicine for a year or two but evidently antagonized the people of the town. At this time he was thirty years of age. He again renewed his acquaintance and editorial activities with the publishers of Lyons and got out a second edition of his Ptolemy and shortly after the Pagnini Bible. This was condemned by the Roman Church and at the time of the Geneva trial Calvin made use of some of Servetus' commentaries on this biblical text as further evidence of his heresy. About 1546 Servetus entered into a correspondence with Calvin over doctrinal beliefs. In 1553 Calvin came, for the second time, into possession of a copy of the "Christianissimi Restitutio", sent him by a Lyons bookseller. Calvin's reaction to the perusal of the book was to denounce Servetus to the ecclesiastical authorities of Lyons by whom he was brought to trial before an inquisitor. He was confined in jail but succeeded in making his escape under circumstances that make it appear that it was accomplished as the easiest way out of a situation that might be embarrassing should the whole history of the matter ever become common knowledge. The authorities, after Servetus' escape, continued their search for the printer of the Restoration of Christianity and when they finally discovered him they burned all the books they found, together with an effigy of the author. Servetus scarcely knew which way to turn but finally took a course that would seem the very last one he would have thought of,—he made his way to Geneva where he remained several days. As he had about made his plans to go on to Zurich he was apprehended through Calvin's orders and brought to trial in the summer of 1553. The trial lasted for several weeks, at the end of which time the judges condemned him to be burned at the stake together with his books. This was done on October 27, 1553, the two volumes that were burned with him, being copies of his "Christianissimi Restitutio", one of them being the book in manuscript just as Servetus had sent it, some eight years before, to Calvin for his comment.

Only three original copies of that work are known to be in existence, one in Paris, one in Vienna and the third in Edinburgh, so that the evidence of this extraordinary man's contribution to medical science rests upon a slender basis. His deductive reasoning in explaining the pulmonary circulation is so clear that it seems strange that others before Harvey's time, less than one hundred years later, should not have drawn the same conclusions. In the parlance of today it probably would be said that Servetus "got what was coming to him". It would seem as though he went out of his way to get into trouble and when once he had clearly defined who were his most powerful enemies he lost no time in "baiting" them. He was anathema in about equal degree to the Catholics and Calvinists and it was only by the assumption of another name, a new profession and a change of residence that he deferred his ultimate fate. When Calvin realized that the author of the "De Trinitatis Erroribus" and the "Christianissimi Restitutio" were one and the same, Servetus was "put on the spot", yet he courted that recognition by deliberately

entering into correspondence with Calvin and he did not have long to wait. There would seem no explanation for his foolhardiness other than that he was conscious of his superiority, intellectually, over his contemporaries and ignored the fact that the enmity that this very superiority aroused would not be content to limit the conflict to the use of intellectual weapons.

MASSACHUSETTS LEGISLATIVE NOTE

THE PROPOSED CHIROPRACTIC BILL

The undersigned qualified voters respectfully petition under Article XLVIII of the amendments to the Constitution governing the popular initiative, viz.: "The Initiative 11, Section 3, for.

"*An Act establishing a Board of Examination and Registration to regulate the Practice of Chiropractic.*"

Be it enacted by the People, and under their authority.

SECTION 1. Chapter thirteen of the General Laws is hereby amended by adding at the end thereof the following sections which sections shall be numbered beginning with the number following the number of the last section in this chapter.

There shall be a board of registration of chiropractors, in this and the two following sections called the board, consisting of three members. Said members shall have been residents of the commonwealth for at least three years, shall be graduates of a legally chartered chiropractic school, college or university having the power to confer degrees in chiropractic, and shall submit a certificate of personal attendance in said school, college or university.

Members of the board shall be appointed by the governor, with the advice and consent of the council for terms of three years. Upon their appointment they shall be deemed to have been duly registered as chiropractors under the provisions of this chapter.

The board shall hold regular meetings to examine applicants and for the transaction of business, commencing on the first Tuesday of June and December, in each year. Special meetings may be called by the chairman and secretary upon thirty days' notice printed in a newspaper of general circulation in the commonwealth. The board shall annually choose a chairman and secretary.

The board shall have authority to administer oaths, take affidavits, summon witnesses and take testimony as to matters pertaining to their several duties, adopt a seal which shall be affixed to all licenses issued, adopt reasonable rules and regulations for the transaction of business and by-laws relating to the enforcement of the provisions of sections which for the purpose of this Act are designated as sections 87T to 87Z9 of Chapter 112 of the General Laws and which shall be numbered in that manner unless through further legislation these numbers have been added to this chapter in connection with added sections in which case these sections shall be renumbered, but the reference to the above numbers shall be construed to apply to the following sections numbered in this act as 87T to 87Z9, of chapter one hundred and twelve of the General Laws.

At the request of the board, an office in the state house where meetings may be held shall be provided.

All fees received by the secretary and not returned to the applicant shall be paid monthly into the state treasury.

Each member of the board shall receive compensation for each day actually spent in the discharge of his duties and also the necessary travelling expenses actually incurred in connection with his duties also the secretary may expend such amounts for books, stationery, postage and other necessary expenses authorized by the board as shall annually be appropriated therefor. Such compensation and expenses shall not exceed in the aggregate the amounts paid into the state treasury as aforesaid.

SECTION 2. Subject to the numbering as provided in section 1, Chapter one hundred and twelve of the General Laws is hereby further amended by inserting at the end thereof under the title Registration of Chiropractors, the following new sections:—

Section 87T. Chiropractic or the system, method or science commonly known as chiropractic, for the purposes of this act shall have the following meaning, namely the science or practice of locating and adjusting by hand the malpositions of the articulations of the human spine. No practitioner of chiropractic, commonly called a chiropractor, shall, unless registered as a physician or surgeon under this chapter, practice obstetrics, or administer drugs or perform surgical operations by the use of instruments, or hold himself out as and for, other than a chiropractor.

Section 87U. The board of registration of chiropractors, in this and the five following sections called the board, may, subject to the approval of the governor and council, make and shall publish necessary rules and regulations for the proper conduct of its duties, shall keep a full record of its proceedings and a record of the names of all persons examined or registered by it. Such rules, regulations and records shall be open to public inspection in the office of the board of registration of chiropractors.

Section 87V. Any person, before engaging in the practice of chiropractic in this commonwealth, shall make application to the board, on a form prescribed and furnished by it, for a certificate to practice chiropractic. Said application shall be filed with the secretary of the board, at least seven days before the date of examination, and shall be accompanied by an examination fee of twenty-five dollars. Each applicant shall present satisfactory evidence in the form of affidavits properly sworn to that he is over twenty-one years of age, of good moral character and has graduated from a reputable chiropractic school, university or college as defined in the following section.

Section 87W. A chiropractic school, university or college shall be considered reputable which possesses the following qualifications:—

First, It shall be incorporated and authorized by its charter to confer the degree of doctor of chiropractic;

Second, It shall give a course of at least twenty-two hundred sixty-minute daylight hours to matriculants possessing the educational qualifications required for graduation from a public high school;

Third, It shall confer such degree only after personal attendance of the applicant therefor at such course, and upon completion thereof.

Section 87X. Any person holding a license or certificate issued by a chiropractic board of any other state maintaining standards at least equal to those of this commonwealth may be registered by the board upon the payment of a fee of twenty-five dollars and the production to the board of his diploma, the certificate or license issued in such other state and satisfactory evidence of good moral character, and thereupon shall be entitled to a certificate of registration.

Section 87Y. The board may refuse to grant a certificate to any person who had been convicted of a felony, who has been guilty of unprofessional conduct, or who is addicted to any vice to such a degree as to render him, in the opinion of the board, unfit to practice chiropractic, and may at any time for cause, after due notice and hearing, revoke a certificate already issued.

Section 87Z. The board shall examine each applicant as to his qualifications for the practice of chiropractic. Such examination may be wholly or in part in writing, and in the English language and shall be of a scientific and practical character, and shall include the subjects of anatomy, physiology, symptomatology, hygiene, sanitation, chemistry, histology, pathology, chiropractic analysis and the principles and practice of chiropractic as taught in reputable chiropractic schools and colleges, and may include practical demonstrations. Any applicant whom the board finds qualified to practice chiropractic shall be registered as a chiropractor by the board and shall receive a certificate of such registration signed by its chairman and secretary.

Section 87Z2. The certificate mentioned in the preceding section shall entitle its holder to practice chiropractic in this commonwealth, shall designate him as a chiropractor and shall be publicly displayed at his principal place of business so long as he shall continue to practice chiropractic.

Section 87Z3. Whoever, without holding a certificate in full force and effect issued by the board, practices or attempts to practice chiropractic in treating diseases of the human body, or uses any of the titles, words or letters, "chiropractic" "chiropractic practitioner", "doctor of chiropractic", "D. C.," or any other titles or letters, either alone or with qualifying words or phrases in such circumstances as to indicate that he is engaged in the practice of chiropractic, or whoever buys, sells or fraudulently obtains any diploma, license, or record of registration to practice chiropractic or aids or abets in same, shall be punished by a fine of not less than fifty nor more than five hundred dollars, or by imprisonment for not less than thirty days nor more than one year, or both.

Section 87Z4. The board shall annually, on or before the first day of January, make a report to the governor containing a full and complete account of all its official acts during the preceding year and setting forth the condition of chiropractic in the commonwealth.

Section 87Z5. Every registered chiropractor, upon commencing to practice, either by himself or associated with or in the employ of another, shall forthwith notify the board of his office address or addresses, and every registered chiropractor practicing as aforesaid shall annually, before April first, pay to the board a license fee of five dollars. Every registered chiropractor shall also promptly notify the board of any change in his office address or addresses and from time to time shall furnish such other information to the board as it may require.

The board may suspend the authority of any registered chiropractor to practice chiropractic for failure to comply with any of the above requirements. The board shall publish annually complete lists of the names and office addresses of all chiropractors registered and practicing in the Commonwealth, arranged alphabetically by name and also by the names of the towns where their various offices are situated.

Section 87Z6. The initial appointments to the board of registration of chiropractors shall, within sixty days after the effective date hereof, be made by the governor, with the advice and consent of the council. One of the said members shall be appointed for the term of one year, one for a term of two years, and the other for the term of three years, and each shall serve until the qualification of his successor.

Section 87Z7. Section seven of said chapter one hundred and twelve, as amended by Statute 1931, chapter 426, is hereby further amended by inserting after the word "gratuitously" the words:— registered chiropractors, so as to read as follows:— Section 7. Sections two to six, inclusive, and section eight shall not be held to discriminate against any particular school or system of medicine, to prohibit medical or surgical service in a case of emergency, or to prohibit the domestic administration of family remedies. They shall not apply to a commissioned medical officer of the United States army, navy or marine hospital service in the performance of his official duty; to an interne or medical officer registered as provided in section nine, while engaged in the practice of medicine as authorized by said section; to an assistant in medicine registered as provided in section 9A, while engaged in the practice of medicine as authorized by said

section; to a physician or surgeon resident in another state who is a legal practitioner therein, when in actual consultation with a legal practitioner of this commonwealth; to a physician authorized to practice medicine in another state, when he is called as the family physician to attend a person temporarily abiding in this commonwealth; nor to registered pharmacists in prescribing gratuitously, registered chiropractors, clairvoyants or persons practicing hypnotism, magnetic healing, mind-cure, massage, Christian science or cosmopathic method of healing, if they do not violate any provision of the preceding sections.

Section 87Z8. Any person who has been a resident of this commonwealth for at least one year next prior to the effective date of this act and has a diploma issued prior to said effective date by a legally chartered chiropractic school, university or college having the power to confer degrees in chiropractic may, within ninety days after such effective date and upon the payment of a fee of ten dollars, apply for a certificate of registration as a chiropractor which certificate may be granted by the board at its discretion without examination.

Section 87Z9. In the event of death of a patient under the care of a chiropractor the said chiropractor shall call the medical examiner of the district where the death occurred.

MISCELLANY

THE COMMITTEE ON PUBLIC RELATIONS

At the last meeting of the Council of the Massachusetts Medical Society a committee on public relations was created apparently with the purpose of studying the relations of the practicing physician and public health procedures. This committee consists of a representative of each of the eighteen districts with the president of the Society as Chairman. The several districts have elected the members composing this committee as follows:

COMMITTEE ON PUBLIC RELATIONS

Barnstable District Medical Society
Dr. John I. B. Vail, Main Street, Hyannis

Berkshire District Medical Society
Dr. P. J. Sullivan, Dalton

Bristol North District Medical Society
Dr. Frank H. Dunbar, Mansfield (P. O. Address —43 Bay State Road, Boston)

Bristol South District Medical Society
Dr. William F. MacKnight, 591 Middle Street, Fall River

Essex North District Medical Society
Dr. W. D. Walker, 121 Main Street, Andover

Essex South District Medical Society
Dr. Harper E. Whitaker, 34 Pleasant Street, Gloucester

Franklin District Medical Society
Dr. J. A. Mather, 58 Federal Street, Greenfield

Hampden District Medical Society
Dr. S. A. Mahoney, 630 Dwight Street, Holyoke

Hampshire District Medical Society
Dr. Francis E. O'Brien, Supt., Hampshire County Sanatorium, Haydenville

Middlesex East District Medical Society
Dr. J. Harper Blaisdell, 5 Bay State Road, Boston (temporary appointee)

Middlesex North District Medical Society
Dr. Joseph Mehan, 4 Park Street, Lowell

Middlesex South District Medical Society
Dr. Charles E. Mongan, 24 Central Street, Somerville

Norfolk District Medical Society
Dr. Walter A. Lane, 173 School Street, Milton

Norfolk South District Medical Society
Dr. William G. Curtis, 10 Grandview Street, Wollaston

Plymouth District Medical Society
Dr. Thomas H. McCarthy, 142 Main Street, Brockton

Suffolk District Medical Society
Dr. Harry W. Goodall, 51 Bay State Road, Boston

Worcester District Medical Society
Dr. Ernest L. Hunt, Worcester City Hospital, Worcester

Worcester North District Medical Society
Dr. Fred R. Dame, 1302 Main Street, Athol

Since some of the members of this committee are not members of the Council and may not have followed the questions raised with respect to "public relations" it will be of advantage to the work of the committee that attention should be concentrated on those problems which are agitating the minds of some of the Fellows and also an articulate group throughout the country.

The conclusions of this committee will be of interest to the profession.

MORTALITY RATES

Telegraphic returns from 82 cities with a total population of thirty-six million for the week ending November 7, 1931, indicate a mortality rate of 10.7 as against a rate of 11.7 for the corresponding week of last year. The highest rate (18.4) appears for New Orleans, La., and the lowest (4.9) for Yonkers, N. Y. The highest infant mortality rate (15.8) appears for Peoria, Ill., and the lowest for Canton, Ohio, St. Paul, Minn., San Francisco, Calif., Lowell, Mass., and Yonkers, N. Y., which reported no infant mortality.

The annual rate for 82 cities is 11.9 for the forty-five weeks of 1931, and the same rate appears for the corresponding weeks of 1930.—*Bureau of the Census.*

COMPARISON OF DISEASE INCIDENCE IN CONNECTICUT WITH 1930 AND SEVEN YEAR AVERAGE

MONTH ENDING NOVEMBER 14, 1931

	1931					1930			
Diseases	Week ending Oct. 24	Week ending Oct. 31	Week ending Nov. 7	Week ending Nov. 14	Average cases reported for week corresponding to Nov. 14 for past seven years	Week ending Oct. 25	Week ending Nov. 1	Week ending Nov. 8	Week ending Nov. 15
Cerebrospinal Men.	1	1	—	—	—	—	—	3	1
Chicken Pox	9	17	32	29	100	22	30	89	73
Conjunctivitis Inf.	—	—	—	—	—	2	—	—	—
Diphtheria	4	5	5	6	35	7	17	6	9
Dysentery Bacillary	1	2	6	—	—	—	1	—	—
Encephalitis Epid.	1	—	—	—	—	—	1	2	1
German Measles	—	—	3	2	2	2	2	1	3
Influenza	4	3	4	3	4	1	3	7	1
Measles	8	9	12	26	41	13	47	55	67
Mumps	12	8	31	20	21	10	18	19	29
Paratyphoid Fever	1	1	1	1	—	—	—	—	—
Pneumonia (Broncho)*	20	6	18	28	16	12	17	18	16
Pneumonia (Lobar)	23	15	20	26	26	12	21	24	19
Poliomyelitis	39	12	17	9	2	3	4	2	2
Scarlet Fever	30	38	27	35	61	16	18	32	38
Septic Sore Throat	—	5	—	1	3	2	1	3	1
Tetanus	1	—	—	—	—	1	—	—	—
Trichinosis (O. F.)	—	—	—	1	—	—	—	—	1
Tuberculosis (Pul.)	28	30	33	16	27	24	19	32	38
Tuberculosis	—	2	2	3	2	2	2	1	3
Typhoid Fever	7	2	4	4	3	7	2	9	3
Undulant Fever†	—	—	—	1	—	—	—	1	—
Whooping Cough	76	47	46	30	63	17	42	59	43
Gonorrhea	22	26	23	65	40	54	30	29	30
Syphilis	45	53	23	43	38	38	52	42	31

Remarks: No cases of Asiatic cholera, glanders, plague and yellow fever during the past seven years.

*Made reportable January 1, 1925.
†Made reportable August 14, 1928.

CORRESPONDENCE

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

535 North Dearborn Street, Chicago, Ill.
November 28, 1931.

Managing Editor, *The New England Journal of Medicine,*

In addition to the articles enumerated in our letter of October 31 the following have been accepted:

Lederle Laboratories, Inc.

Diphtheria Toxin-Antitoxin Mixture, 0.1 L+ (Goat)

H. K. Mulford Co.

Ivyol-Poison Oak Extract-Mulford

Hypo Units Ivyol-Poison Oak Extract

U. S. Standard Products Co.

Typhoid Vaccine, one 5 cc. vial package

Typhoid Vaccine, one 20 cc. vial package

Typhoid Paratyphoid Vaccine Combined, one 5 cc. vial package

Typhoid Paratyphoid Vaccine Combined, one 20 cc. vial package

The following article has been exempted and included with the List of Exempted Medicinal Articles (New and Nonofficial Remedies, 1931, p. 477):

Lederle Laboratories, Inc.

Ferric Ammonium Citrate-Lederle capsules, 0.5 Gm.

Yours truly,
W. A. PUCKNER, *Secretary,*
Council on Pharmacy and Chemistry.

OBITUARY

RESOLUTIONS BY THE MASSACHUSETTS PSYCHIATRIC SOCIETY ON THE DEATH OF ELISHA H. COHOON

By the death of Dr. Elisha H. Cohoon there has been lost to psychiatric service, to numberless patients, to numerous employees and to loving friends

a great administrator,—a tireless servant,—a justly respected employer, and a most devoted friend.

Dr. Cohoon, born in Nova Scotia fifty-seven years ago, graduated from Acadia University, N. S., and received his medical education in Baltimore, Md., graduating from the College of Physicians and Surgeons. He joined the staff of the State Hospital at Mt. Pleasant, Iowa, for three years, then served a year at the Colorado State Hospital at Pueblo.

The next seven years he spent at the State Hospital at Howard, R. I., where he firmly established a reputation as a successful executive. He was called to serve as administrator of the Boston Psychopathic Hospital for a period of two years, leaving there to accept the superintendency of the Medfield State Hospital, Medfield, on April 1, 1917.

At Medfield Dr. Cohoon brought a keen knowledge of psychiatry, an understanding interest to the welfare of his patients, and a deep sense of justice to all, both patients and employees. His courteous attitude toward the public was another distinguishing mark of a truly great man. Medfield State Hospital received the benefit of numerous carefully planned and executed innovations and improvements for the care and welfare of its patients. Dr. Cohoon introduced new facilities for treatment according to the best of methods and established many forms of physical comforts and entertainments for his patients. His employees knew him to be the gracious employer, tolerant, and, above all, just in every respect. In the community much of his time was freely given to addresses before civic organizations of all sorts. Especial attention was given to out-patient clinics in nearby towns.

After a lingering illness, death claimed Dr. Cohoon on July 21, 1931, while a patient at a Boston hospital. He was a member of the Massachusetts Medical Society, American Psychiatric Society, and of the New England Society of Psychiatry. At the time of his death Dr. Cohoon was president of the Massachusetts Psychiatric Society. The members of this society who knew him so well and loved him so genuinely have sustained a severe loss of counsellor and friend. This society may well be proud of his record, mourn his loss and, in reverence, pay its respects to the passing into the Great Adventure of a truly great physician.

NEWS ITEMS

DR. H. WARREN CROWE WILL VISIT THE UNITED STATES—Dr. H. Warren Crowe, D.M., B.Ch. (Oxon.), M.R.S.C., L.R.C.P. of England, will visit this country shortly for the purpose of lecturing at the Conference on Rheumatism which is to be held at Pittsburgh. Dr. Crowe is the author of "Vaccine Treatment of Chronic Rheumatic Diseases", "The Treatment of Chronic Arthritis and Rheumatism" and "Bacteriology and Surgery of Chronic Arthritis and Rheumatism" (Oxford University Press).

PROFESSOR DRINKER AND LOUIS A. SHAW HONORED—The gift to mankind by the invention of the modern Respirator by Professor Philip Drinker and Louis A. Shaw has been recognized by the presentation of the John Scott Medals for 1931 at the Franklin Institute, Philadelphia. This apparatus has saved the lives of many victims of poliomyelitis and gas poisoning. It is one of the important contributions to life-saving apparatus.

NOTICES

MEDICAL CLINIC AT THE PETER BENT BRIGHAM HOSPITAL

At 3:30 P. M., on Thursday, December 10, in the Amphitheatre of the Peter Bent Brigham Hospital, a medical clinic will be given by Dr. Henry A. Christian, to which physicians are cordially invited. The clinics will be held regularly on Thursday afternoons.

UNITED STATES CIVIL SERVICE EXAMINATIONS

Senior Medical Officer, $4,600 a Year
Medical Officer, $3,800 a Year
Associate Medical Officer, $3,200 a Year

Applications must be on file with the U. S. Civil Service Commission at Washington, D. C., not later than December 30, 1931.

In the absence of further notice, applications for these examinations will be received until the date given above. After 30 days from the date of the issuance of this announcement, applications will be rated as received and the names of eligibles will be placed on the register in the order of their relative standing, with credit for military preference, if any. Certification will be made as the needs of the service require. The Commission reserves the right to issue subsequent notice closing the receipt of applications before the date named above.

RADIO HEALTH MESSAGES

Sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

Courtesy WBZA. Thursdays at 5:17 P. M.

December

10 Can We Prolong Life?
17 Pasteurized or Raw Milk
24 Public Health in the Coming Year
31 Mental Health

STATE HOUSE BROADCAST

Sponsored by the Massachusetts Department of Public Health.

Courtesy WEEI. Fridays at 12:30 P. M.

The various activities of the Department are discussed by the Directors of its nine Divisions.

RADIO HEALTH FORUM

Directed by the Massachusetts Department of Public Health.

Courtesy WEEI. Fridays at 4:50 P. M.

Queries from the public are answered under the sponsorship of the Department.

Questions on Health and Prevention of Disease may be sent to: Radio Health Forum, State Department of Public Health, State House, Boston.

PROGRAM

SPECIAL SERIES OF BROADCASTS

Sponsored by the Massachusetts Department of Public Health. Courtesy WEEI. Mondays at 7:15 P. M.

Health from Zero to Ninety

December

7 Health and Safety of the Young Adult
C.-E. A. Winslow, Ph.D.

14 Health At and After the Prime of Life
Herbert L. Lombard, M.D.

WHITE HOUSE CONFERENCE ON CHILD HEALTH AND PROTECTION

Round Tables

December

21 Round Table No. 1—Why Another Conference?
Conducted by George H. Bigelow, M.D.

28 Round Table No. 2—How Much Care Does the Well Child Need?
Conducted by Mr. Frank W. Kiernan

1932

January

4 Round Table No. 3—Health in Education—Education in Health
Conducted by Raymond Patterson, Ph.D.

11 Round Table No. 4—What a Community Owes to Its Children
Conducted by Lila Owen Burbank, M.D.

18 Round Table No. 5—Unto the Least of These
Conducted by Mr. Alfred F. Whitman

REPORTS AND NOTICES OF MEETINGS

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society was held in the Peter Bent Brigham Hospital on the evening of November 10. Dr. Harvey Cushing presided.

The surgical case was presented by Dr. D. V. Troppoli as follows: A forty-seven-year-old American housewife entered the hospital because of a dull epigastric pain. The family history is interesting in that her mother died of cancer of the stomach. A sister died of gastric ulcer at the age of twenty-five. Seven weeks before admission she first experienced a dull aching epigastric pain, which came on at any time during the day but never at night and was always immediately relieved by food. At the same time she had a sense of fullness after eating her usual meals, so that she was taking six or eight small meals each day. There was never any nausea or vomiting, nor did she notice any melena. Two weeks before admission she noticed a movable, non-tender, epigastric mass. Physical examination on admission was essentially negative except for this mass. The red count was 4,100,000 and the hemoglobin was 60%. X-ray examination revealed a filling defect occupying the middle third of the lesser curvature of the stomach. Gastric analysis showed a free acid of 14 and a total acid of 50. Dr. David Cheever operated upon the patient and did a total gastrectomy and an esophagojejunostomy. A jejunal tube was left in place for temporary feeding. Pathologic examination shows practically complete involvement of the excised stomach. Convalescence has been fairly uneventful. On the third day fluids were given through the jejunal tube and small amounts were given by mouth on the sixth day. She is now taking soft solids by mouth. Hydrochloric acid has been given daily although no symptoms of pernicious anemia have developed.

Dr. Cheever briefly discussed the technic of the operation which is the first of total gastrectomy done at the Peter Bent Brigham Hospital. Only seventy-two are reported in the literature. The operation is unusual because it is rare to find a malignant process so extensive that such a radical procedure is justified and yet without any evidence of metastasis.

Dr. Selwyn Steele presented the medical case, that of a forty-nine-year-old American housewife who entered the hospital because of fever and malaise of eight weeks' duration. Thirty, twenty, and five years ago she had attacks of phlebitis in the right leg. Eight weeks before entry it recurred and ran an unusual course for two weeks. A mild fever and general malaise continued, however, and after two weeks she was forced to return to bed and finally came to the hospital. Physical examination was essentially negative except for a definitely enlarged liver. The white count was 4,000, the red count 4,000,000 and the hemoglobin 60%. Liver and renal function tests were normal. Stool and blood cultures were negative as was the Widal test. For the first week her temperature ranged from 100 to 103. Agglutination with Brucella melitensis was positive in dilutions up to 1-1215; this established the diagnosis of undulant fever. During the second and third weeks the temperature assumed a downward trend ranging from 99° to 101° but it has since risen and now fluctuates between 100° and 103°.

Dr. Alexander Forbes spoke on "An Expedition to Northern Labrador" describing some of his experiences while making a geographical survey of a portion of that territory during the past summer.

Sir Wilfred Grenfell, K.C.M.G., spoke on "Medical Practice in the Labrador." He discussed the country and its people and told of many of his interesting medical experiences during his forty years of active service in Labrador.

MASSACHUSETTS PSYCHIATRIC SOCIETY

On October 30, 1931, the annual meeting of the Massachusetts Psychiatric Society was held at the Hotel Somerset. The address of the evening was made by Charles Slocombe, Ph.D., on "The Scientific Method in Motor Vehicle Administration."

The following officers for the ensuing year were selected:

A. Warren Stearns, M.D., President.

Winfred Overholser, M.D., Secretary and Treasurer.

Morgan B. Hodskins, M.D., Vice-President.

Oscar J. Raeder, M.D. and Kenneth J. Tillotson, M.D. Councillors.

Resolutions were adopted by the Society at this meeting on the death of Dr. Elisha H. Cohoon, who at the time of his death was president of the Society*.

WINFRED OVERHOLSER, *Secretary.*

*See page 1123.

THE ROXBURY CLINICAL RECORD CLUB

On November 17 the Roxbury Clinical Record Club held its regular meeting in the Harvard Club.

The central subject of this meeting was a consideration of matters affecting public health administration in its relation to the care of certain types of illness. In introducing the subject the President of the Club, Dr. Harvey P. Towle, called attention to the very large number of clinics and health centers under voluntary and official administration and introduced Dr. Robert B. Osgood to discuss the problems incident to rheumatism which is one of the perplexing medical subjects of the day which seems to demand study by clinicians and health departments.

Dr. Osgood gave a scientific discourse dealing particularly with the chronic forms of rheumatism as they come under the care of the orthopedic surgeon with explanations of the etiology and management of these disabling infirmities. He was insistent on the necessity of the earliest possible treatment of those forms of so-called rheumatism which tend to become chronic with the comforting assurance that much can now be done to ameliorate the condition and even bring about cure if the efforts of the surgeon are augmented by loyal coöperation of the patient. In this address Dr. Osgood presented his latest opinions and conclusions with reference to this disease and it is expected that it will be given to this *Journal* for publication.

He was followed by Dr. William H. Ross, Ex-President of the New York State Medical Society, who practically abandoned his professional work during his presidency in order that he might bring his Society into a more united body in the promotion of more effective coöperation of the practitioners and health departments of New York State. It is generally recognized in New York that Dr. Ross' administration brought about the almost unanimous support of the profession of that State in advanced public health administration. The response to the work done by Dr. Ross stands as a demonstration of the possibilities of the effective influence of organized medicine under enthusiastic and sound leadership. We hope to secure a digest of Dr. Ross' paper for publication.

These addresses were introductory to that of the next speaker, Dr. George H. Bigelow, Commissioner of Health of Massachusetts, who gave an elaborate explanation of the activities of his department, dealing especially with those features which are designed to be of service to the clinician whenever the wish is expressed for counsel or technical aid. He expressed the conviction that practitioners and departments of health must always maintain the most cordial relations, each group striving to understand the aims, purposes and functions of the other and that any differences of opinion about details which would lead to antagonism is unthinkable because both groups are dedicated to the service of humanity.

A very general discussion followed by the members and guests of the club and it was voted that the President appoint a committee of five members who would consider the subjects discussed and report to future meetings any recommendation which might be deemed of interest.

EXCERPTS FROM THE GEORGE W. GAY LECTURE BY DR. JOHN M. BIRNIE

Dr. John M. Birnie of Springfield, Mass., gave the second of the George W. Gay lectures on Medical Ethics for this year at the Harvard Medical School on the afternoon of November 18. Dr. Gay was appalled at the number of physicians who became financially dependent in later life and for this reason Dr. Birnie spoke on "Independence for the Doctor."

The physician, realizing that a financier's advice on medical matters is usually worthless, should also realize that his own judgment on financial matters is often of no greater value and that business and finance must of necessity be subsidiary issues in his life because of the press of professional duties.

The three basic rules that will almost certainly lead to financial independence are to work hard, to save systematically, and to make the savings work for you. The physician should establish the reputation of being ready and willing to serve the public at any time. He should always be available within a few hours' time. Dr. Birnie especially advises against the young doctor taking one afternoon a week for recreation and suggests that he wait for a quiet afternoon and even then remain on call. Hard conscientious work will build a practice. It is then necessary to save. Investments such as stocks, bonds and real estate cannot be considered savings but are simply gambles and the doctor is notorious for his failures. Rather the young doctor should immediately begin to save a definite percentage of his gross income by depositing it in a savings or coöperative bank or by buying insurance. Dr. Birnie outlined each of these systems and discussed their relative merits. In each way one's money is constantly working for him thus fulfilling the third basic rule. Dr. Birnie advises saving

twenty per cent. of the gross income, except perhaps during the first few years of practice when this amount may be too large. However, the young doctor should begin to save immediately although the amount may be small. Delay almost invariably means that systematic saving will never be established.

Above all, speculation in any form is absolutely precluded from this system. The doctor should choose his financial adviser as carefully as the layman should choose his physician and should ignore all offers which promise something for nothing. By training himself to spend less than he earns a doctor can learn the secret of obtaining financial independence in the later years of his life.

PLYMOUTH DISTRICT MEDICAL SOCIETY

The November meeting of the Plymouth District Medical Society was held at the Moore Hospital in Brockton on Thursday, November 19, 1931. The meeting was opened by Dr. John J. McNamara, president of the Plymouth District Society. He gave a short address of welcome to the large number of physicians and surgeons from all over Plymouth, Norfolk, and Bristol counties. Dr. Moore showed some very interesting moving pictures for the entertainment of the members of the Society. The business meeting followed. The records of the last regular meeting were read by Dr. George A. Moore, secretary of the society. They were approved. During the business meeting Dr. Frederick F. Weiner of the Brockton Hospital asked for information about the chiropractic bill that is to come up at the next session of the Massachusetts Legislature. Dr. McNamara said that he thought Dr. Thomas H. McCarthy was more familiar with the chiropractic bill and was better informed than any other physician connected with the Society. He called on Dr. Thomas H. McCarthy, Vice-President of the Massachusetts Medical Society, to tell the Plymouth District Society what he knew about the activities of the chiropractors. Dr. McCarthy said that the chiropractors were going to make their greatest effort this year. Their intention is to have a special board for the examination of chiropractors. It has been suggested that the board would consist of three persons to be appointed by the Governor to pass upon the qualifications of applicants desiring to practice chiropractic. These applicants must have had a preliminary education to that required for graduation from a High school and be grounded in the subjects of physiology, anatomy, chemistry, hygiene, sanitation, pathology and chiropractic analysis. There has been but one standard for the qualification of fitness to practice the healing art in this Commonwealth, namely, passing the examination given by the board of registration in medicine. This method has been acceptable to the homeopaths, osteopaths and members of the regular school of medicine. The Medical Society feels it would be a definite step backward to change this policy. The official stamp of approval is thus placed upon every legalized practitioner of medicine in the State of Massachusetts, and if a minor or a stranger calls a registered physician in an emergency, the public realizes that the physician has been examined and authorized to alleviate suffering and treat disease. If cultists are to be permitted to practice and their school does not teach diagnosis and treatment by accepted methods, grave dangers may result by the failure to recognize communicable diseases. A very important objection to the licensing of cultists is the inadequate attention paid to public health problems by the institutions from which they have graduated, and consequently they may not fit such practitioners to coöperate effectively with the State Department of Health. You have all heard about the initiative and referendum. The chiropractors have tried the referendum but they have failed. Now they are going to try the initiative. They have a large number of paid workers in each community, even right here in Brockton. They intend to get 15,000 names so that they can put their bill directly before the legislature. These paid workers are mingling among the people all the time in an energetic effort to get the required names. I want to tell you gentlemen and in fact every physician all over the state that if we do not take more interest in what is going on around us in regard to the chiropractors and their methods, something drastic is going to happen. I believe that the whole trouble with the members of this society is that they are too selfish. They are continuously thinking about themselves and not about what might happen to the other fellow. We must work as a body and individually. Every member of this society must do a little work or the chiropractors will succeed. We must make the greatest effort to stop this bill from going through. If this measure is passed, you will find in every second block in Brockton, and in fact all over the state, one of these persons doing business in competition with us. If we do not work as a body, we are lost. All of us must coöperate in this movement because we cannot prevent it by publicity alone. It will go before the great and general court as an initiative. It won't be long now before we will have our annual meeting with the legislators of this district, our senator and the representatives. We had a wonderful meeting at the Commercial Club last year. All of the representatives and the senator were there. We explained to them at that time the different bills in which we were interested. We gave them all full information so that they might better understand the features of every public health bill. We know that the laymen, and in fact any person not connected with the medical profession, are unfamiliar with medical legislation. We simply want to be fair about this proposition. If each and every district would do what the Plymouth District has been doing the Senators and Representatives all over the state would know and understand what these bills mean. No bill would then be

enacted if every senator and representative had a clear understanding of what all these medical bills mean. I have found in the past that all of our legislators are fair if they thoroughly understand that these various medical bills are detrimental to the public. They usually support any reasonable bill. If we recommend that a bill be passed they usually do it by their vote, but if pernicious influences are working against us all the time and these influences tend to tear down instead of to build up, our society will surely suffer. I sincerely hope that each and every one will get behind and prevent this latest move of the chiropractors. In closing I want to say that our Council has praised the Plymouth method of these "get together meetings". We look forward each year to a meeting of this kind which we always consider a very enjoyable "get together". Dr. McCarthy received cordial applause for his speech.

The society then accepted an invitation from Dr. Peirce H. Leavitt to hold the March meeting at the Goddard Hospital. Dr. McNamara called upon the different members of the society to present cases. The first to respond was Dr. John H. Weller, assistant medical director of the Bridgewater State Hospital, who described two cases of aneurism, one of the right iliac artery and the other of the axillary artery. Both reports were extremely interesting. Dr. Leonard A. Baker of Middleboro reported a very interesting case of rupture of the bladder following a second operation of cesarean section. Dr. Arthur W. Carr of Bridgewater reported a case of gangrenous Meckel's diverticulum. Dr. Carr's remarks were very well chosen. Dr. John J. Condrick of Brockton reported several cases of Acute Infections of the Lip and Face. Dr. Condrick showed a patient that had been treated by the diathermy method without any operation. The patient showed a very good result and recovery. Dr. John Noyes discussed acute infections of the face. Dr. George A. Moore also discussed infections of the face and how they were treated at the Moore Hospital. All of these cases that were shown were handled in coöperation with Dr. George A. Moore, chief surgeon of the Moore Hospital. Dr. McNamara, president of the society, thanked all the physicians who presented these cases, in behalf of the society. Dr. McNamara said, "We are trying to interest all of the physicians of the district to bring cases of interest to the members because it is only by this method that we can improve ourselves. Any physician who finds an interesting case should present it."

Dr. McNamara then introduced the principal speaker of the day, Dr. E. Parker Hayden one of the surgeons of the Massachusetts General Hospital, who took for his subject "Diseases of the Small and Large Intestine and Rectum and Their Treatment." Dr. Hayden discussed this subject in a very thorough manner. He showed numerous moving pictures from a machine operated by Mr. Arthur M. Keith. These pictures showed the work that he had been doing and the result of each operation. Treatment of the cases of carcinoma of the large intestine and rectum were followed by excellent results. His address was very much appreciated. A rising vote of thanks was given Dr. Hayden for his excellent talk and demonstration.

A fine wild duck luncheon was served by Dr. George A. Moore. It was supervised by his secretary Isabelle Packard. There were over 60 physicians and surgeons present at this meeting.

THE WILLIAM HARVEY SOCIETY

Friday, December 11, 1931, 8:00 P. M. at the Beth Israel Hospital.

Speaker: Dr. Hans Zinsser, Professor of Bacteriology and Immunity, Harvard Medical School.

Subject: Typhus Fever and Allied Diseases, Their History and the Present State of Our Knowledge Concerning Them.

Chairman: Dr. Joseph Hersey Pratt, Professor of Clinical Medicine, Tufts College Medical School.

MASSACHUSETTS GENERAL HOSPITAL

A Clinical Meeting of the Staff of the Massachusetts General Hospital will be held in the Moseley Memorial Building, on Thursday, December 10, at 8:15 P. M.

PROGRAM

1. Evaluation of Surgical Risk from the Viewpoint of an Internist. Dr. Arlie V. Bock.
2. Nutritional Edema as a Postoperative Complication. Dr. Chester M. Jones.
3. Prevention of Postoperative Pulmonary Complications. Dr. Donald King.

Discussion will be opened by Dr. Lincoln Davis and Dr. Edward D. Churchill.

Physicians, medical students and nurses are cordially invited to attend.

COMMITTEE ON CLINICAL MEETINGS.

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

Meeting at the Copley-Plaza, Wednesday, December 9, 1931. Dinner, 6:45 P. M. $2.50 per plate.

Communications:

Dr. E. A. Codman: Normal Motions of the Shoulder Joint.

Dr. P. D. Wilson: Injuries of the Capsule of the Shoulder Joint.

Dr. Russell Sheldon: Anesthesia, Past, Present, and Future

Discussion after Dr. Sheldon's paper opened by Dr. Frank L. Richardson.

W. A. BISHOP, M.D., *President*.
W. P. COUES, M.D., *Secretary*.

HARVARD MEDICAL SOCIETY

Next meeting in the Peter Bent Brigham Hospital Amphitheatre (Van Dyke Street entrance), Tuesday evening, December 8, at 8:15 o'clock.

PROGRAM

Presentation of cases.

The Evolution of the Babinski Response as Illus-

trated in the Monkey, Baboon, and Chimpanzee. (With motion pictures.) By Dr. John Fulton, Professor of Physiology, Yale Medical School.

Medical students and physicians are cordially invited to attend.

JOHN HOMANS, *Secretary.*

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the office of the Boston Tuberculosis Association, 554 Columbus avenue, Boston, on Tuesday, December 15, 1931, at 12 noon.

The speaker will be Dr. Hilbert F. Day, Surgeon-in-Chief, New England Medical Centre; Professor of Clinical Surgery, Tufts Medical School; and his subject, "Treatment of Enlarged Veins of the Lower Extremity."

The usual luncheon will be served at 1 o'clock. All physicians are cordially invited to attend.

THE NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular quarterly meeting of the New England Dermatological Society will be held on Wednesday, December 9. There will be a clinical meeting at the Skin Out-Patient Department of the Boston City Hospital at three P. M.

WM. P. BOARDMAN, *Secretary,*
New England Dermatological Society.

SUFFOLK DISTRICT MEDICAL SOCIETY

The December meeting of the Suffolk District Medical Society will be a clinical meeting to be held at the Peter Bent Brigham Hospital, 721 Huntington Avenue, Boston, on Wednesday, December 16, 1931, at 8:15 p. m.

CLINICAL PROGRAM

1. Medical Clinic—Dr. H. A. Christian.
2. X-ray Conference—Dr. M. C. Sosman.
3. Surgical Clinic—Dr. Harvey Cushing.

GEORGE S. DERBY, M.D., *President.*
LELAND S. MCKITTRICK, M.D., *Secretary.*

GREATER BOSTON MEDICAL SOCIETY

A joint meeting of the Greater Boston Medical Society and the Beth Israel Hospital will be held on Wednesday, December 9, at 8:15 P. M., at the Beth Israel Hospital.

Program:

Intravenous Urography as a Diagnostic Aid. Moses Swick, M.D., New York City.

Practical Applications of Intravenous Pyelography. H. Granville Crabtree, M.D.

Discussion. George Prather, M.D., Boris E. Greenberg, M.D. and Samuel A. Robins, M.D.

BERNARD I. GOLDBERG, M.D., *Secretary.*

WORCESTER DISTRICT MEDICAL SOCIETY

The next meeting will be held December 9, 1931, at 7:30 P. M. at the Chamber of Commerce Building, Worcester.

Program:

(a) Glaucoma:—Dr. Albert E. Cross, Worcester, Mass.

(b) Some Complications of Acute Upper Respiratory Infections:—Dr. Armand L. Caron, Worcester, Mass.

(c) Convalescence after Tonsillectomy, Dr. Harold Gibby, Worcester, Mass.

(d) Chronic Upper Respiratory Infections with special reference to the Maxillary Sinuses and Subadjacent Teeth, Dr. Gordon Berry, Worcester, Mass.

E. C. MILLER, M.D.

SOCIETY MEETINGS
CONGRESSES AND CONFERENCES

December 8—Harvard Medical Society. See page 1128.

December 9—The New England Dermatological Society. See notice elsewhere on this page.

December 9—Massachusetts Society of Examining Physicians. See page 1128.

December 9—Greater Boston Medical Society and the Beth Israel Hospital. See notice elsewhere on this page.

December 10—Medical Clinic at the Peter Bent Brigham Hospital. See page 1124.

December 10—Massachusetts General Hospital. See page 1128.

December 11—The William Harvey Society. See page 1128.

December 11—New England Pediatric Society. See notice on page 1030, issue of November 19.

December 15—South End Medical Club. See notice elsewhere on this page.

December 18—The Boston City Hospital Clinic. See page 1072, issue of November 26.

January 6 - June 1—New England Heart Association. See page 891, issue of October 29.

April 4-8, 1932—The American College of Physicians. See notice on page 1232, issue of June 4.

Autumn 1931—Spring 1932—International Medical Postgraduate Courses in Berlin. See page 468, issue of August 27.

DISTRICT MEDICAL SOCIETIES

Essex North District Medical Society

January 6, 1932—At Haverhill.

May 4, 1932—Annual meeting at Lawrence.

Essex South District Medical Society

January 6, 1932, Wednesday—Danvers State Hospital, Hathorne. Clinic 5 P. M. Dinner 7 P. M. Speaker: Dr. Harry Solomon, Boston. Subject: Modern Treatment of Syphilis.

February 3, 1932, Wednesday—Council Meeting, Boston.

February 10, 1932, Wednesday—Hawthorne Hotel, Salem. Dinner 7 P. M. Speakers: Dr. Lincoln F. Sise and Dr. Harry H. Germain. Subject: Selection of the Anesthetic for the Patient and Operation. Dr. Sise to speak from the viewpoint of the Anesthetist, and Dr. Germain from the viewpoint of the Surgeon.

March 2, 1932, Wednesday—Lynn Hospital. Clinic 5 P. M. Dinner 7 P. M. Subject to be announced later. Speaker: Dr. Elmer W. Barron, Boston.

April 6, 1932, Wednesday—Essex Sanatorium, Middleton. Clinic 5 P. M. Dinner 7 P. M. Speaker: Dr. Arthur P. Wakefield, State Department of Health. Subject: 10-Year Tuberculosis Program in the Public Schools.

May 5, 1932, Thursday—Censors' Meeting, Salem Hospital, 3:30 P. M.

May 10, 1932, Tuesday—Annual Meeting. The Tavern, Gloucester. Speaker and subject to be announced later. Ladies invited.

Franklin District Medical Society

Meetings will be held on the second Tuesday of January, March and May at the Weldon, Greenfield, at 11 A. M.

CHARLES MOLINE, Secretary.

Middlesex East District Medical Society

At a meeting of the executive committee the following schedule for the Middlesex East District Medical Society was arranged:

January—At Melrose.

March—At Reading.

May—At Woburn.

All meetings on the second Wednesday of each month unless otherwise announced.

Middlesex South District Medical Society

December 10—See page 1076, issue of November 26.

Norfolk District Medical Society

January 26, 1932—Boston Sanatorium, Mattapan. Dr. Timothy J. Murphy. Meeting to be devoted to Diseases of the Chest.

February 23, 1932—Place to be announced. Clinico-Pathological meeting, Dr. Frank S. Cruickshank, Dr. F. B. Mallory, or a representative from his department.

March 29, 1932—Place to be announced. Boston Public Health Meeting. Speakers, Honorable James M. Curley, Dr. Francis X. Mahoney, Dr. Charles Wilinsky, Dr. W. H. Griffin.

May, 1932—Annual Meeting, date and place to be announced.

May 5, 1932—Censors' Meeting for examination of candidates. Roxbury Masonic Temple, 171 Warren Street, Roxbury, 4 P. M. Fee $10.00 payable at time of examination. All candidates will have applications in the hands of the secretary one week prior to this date. All candidates from Medical Schools not on approved list of Society must have application complete two weeks prior to date of examination.

F. S. CRUICKSHANK, Secretary.

Norfolk South District Medical Society

December 3—Speaker: George H. Bigelow, M.D., Commissioner of Public Health. Subject: Some Communicable Disease Control Problems.

January 7—Speaker: William Reid Morrison, M.D. Subject: Stomach Surgery.

February 4—This meeting will be held at the Quincy City Hospital. The program will be furnished by the members of the hospital staff.

March 3—Speaker: Roderick Heffron, M.D. Subject: Pneumonia.

April 7—To be announced later.

May 5—Annual meeting.

The time of all meetings is 12 o'clock noon. All meetings, except February 4, will be held at the Norfolk County Hospital, South Braintree. Censors will meet on May 5 at 11:15 A. M. at the Norfolk County Hospital.

N. R. PILLSBURY, Secretary.

Suffolk District Medical Society

December 16, 1931—Clinical Program, Peter Bent Brigham Hospital. See page 1129.

January 27, 1932—General Meeting in Association with the Boston Medical Library. Titles and speakers to be announced later.

February 24, 1932—Clinical Program, the Children's Hospital.

March 30, 1932—Clinical Program, New England Deaconess Hospital.

April 27, 1932—The Annual Meeting, Boston Medical Library. Election of Officers.

The Medical Profession is cordially invited to attend all of these meetings.

GEORGE S. DERBY, M.D., President.
LELAND S. McKITTRICK, M.D., Secretary.
HILBERT F. DAY, M.D., Boston Medical Library.

Worcester District Medical Society

Wednesday evening, December 9, 1931—See page 1129.

Wednesday evening, January 13, 1932—Worcester City Hospital, Worcester, Mass. 6:30—Dinner, complimentary by City Hospital. 7:45—Program: To be announced later.

Wednesday evening, February 10, 1932—Worcester State Hospital. 6:30—Dinner, complimentary by the Worcester State Hospital. 7:45—A psychiatric program to be announced later.

Wednesday evening, March 9, 1932—Memorial Hospital, Worcester, Mass. 6:30—Dinner, complimentary by Memorial Hospital. 7:45—A pediatric meeting with subjects to be announced later.

Wednesday evening, April 13, 1932—Grafton State Hospital, North Grafton, Mass. 6:30—Dinner, complimentary by Grafton State Hospital. 7:45—Program to be announced later.

Wednesday afternoon and evening, May 11, 1932—Annual Meeting. Program to be announced later.

ERWIN C. MILLER, Secretary.

BOOK REVIEWS

Tables of Food Values. By ALICE V. BRADLEY. The Manual Arts Press, Peoria, Illinois. 128 pp. Price $2.00.

This well-bound and well-printed little book gives a set of 50 tables in which the calorie, mineral and vitamin values of all the common foods are presented with the ordinary serving as the unit. The relative values of each food as a source of bulk and its ultimate end or basic reaction are also shown. In addition recipes under each class of food are included. The tables are preceded by an explanation of their use and a discussion of some of the fundamental and modern ideas regarding diet.

We are only beginning to make practical use of the tremendous amount of new knowledge regarding the importance of the minerals and final reaction of the components of the diet. This book should be most useful to physicians and dietitians in planning diets.

Simple Lessons in Human Anatomy. By B. C. H. HARVEY, M.D., Professor of Anatomy, University of Chicago. Published by the American Medical Association, 1931. Price $2.00.

In his preface to this book, Dr. Fishbein explains that it was prepared by Dr. Harvey as a series of articles for *Hygeia*, the health magazine published by the American Medical Association. It constitutes a descriptive human anatomy for the layman combined with a considerable discussion of physiology and hygiene. It is illustrated admirably by a series of 234 text cuts, many of them of historical interest. As a frontispiece is published an interesting colored German chart representing the human body as a factory. The endorsement which its publication gives to this book is sufficient evidence of its merit and it should have a unique value in the dissemination of desirable anatomic and physiologic knowledge among those who would otherwise be likely not to obtain it or to obtain it in less satisfactory form.

Surgical Pathology of the Genito-Urinary Organs. By ARTHUR E. HERTZLER, M.D. J. B. Lippincott Company. Price $5.00.

This is one of a series of monographs on surgical pathology by Dr. Hertzler, professor of surgery at the University of Kansas.

In the opening chapter of the book the author says, "The inflammatory diseases, chiefly venereal, of the penis, even in this day of specialization are cared for mostly by the drug store doctors and the quacks. Urologists disdain this kind of patient." The reviewer, although a urologist, does not disdain this kind of patient, but does not believe the attitude of the average urologist toward the unfortunate victim of venereal disease is one of disdain.

The book is very readable, profusely and well illustrated, and gives one a rapid review of the pathology and histology of the genito-urinary organs.